COMPARISON OF THE DURATION OF ANALGESIA, DURATION OF SENSORY AND MOTOR BLOCKADE AND INCIDENCE OF SIDE EFFECTS OF INTRATHECAL 0.75% ISOBARIC ROPIVACAINE WITH COMBINATION OF 0.75% ISOBARIC ROPIVACAINE AND DEXMEDETOMIDINE FOR LOWER LIMB ORTHOPAEDIC SURGERIES

Dissertation submitted in partial fulfillment of
M.D. DEGREE EXAMINATION
M.D. ANAESTHESIOLOGY- BRANCH X
CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI, TAMILNADU.
APRIL 2013

CERTIFICATE

This is to certify that the dissertation entitled, **"COMPARISON OF THE DURATION OF ANALGESIA, DURATION OF SENSORY AND MOTOR BLOCKADE AND INCIDENCE OF SIDE EFFECTS OF INTRATHECAL 0.75% ISOBARIC ROPIVACAINE WITH COMBINATION OF 0.75% ISOBARIC ROPIVACAINE AND DEXMEDETOMIDINE FOR LOWER LIMB ORTHOPAEDIC SURGERIES"** submitted by Dr.VIJAYANAND,K. in partial fulfillment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamilnadu Dr. M.G.R. Medical University, Chennai is bonafide record of the work done by him in the CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU, during the academic year 2011-2013.

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DECLARATION

I, **Dr. K.Vijayanand**, solemnly declare that the dissertation **COMPARISON OF THE DURATION OF ANALGESIA, DURATION OF SENSORY AND MOTOR BLOCKADE AND INCIDENCE OF SIDE EFFECTS OF INTRATHECAL 0.75% ISOBARIC ROPIVACAINE WITH COMBINATION OF 0.75% ISOBARIC ROPIVACAINE AND DEXMEDETOMIDINE FOR LOWER LIMB ORTHOPAEDIC SURGERIES"** is a bonafide work done by me in the Department of Anaesthesiology, Chengalpattu Medical College & Hospital, Chengalpattu, after getting approval from the Ethical committee under the able guidance of **Prof. Dr. V.JAYARAMAN M.D.D.A.,** Professor & HOD, Department of Anaesthesiology, Chengalpattu Medical College, Chengalpattu.

Place : Chengalpattu

Date : **(Dr. K.Vijayanand)**

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Dated:12.10.2012.

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Ref: 1) Application dated: 18.07.2012of the Individual.
2) Letter dated 18.07.2012 of the Head of the Department of Anaesthesiology, Chengalpattu Medical College,Chengalpattu.

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Dr.K.Vijay Anand, Post Graduate Student in M.D.(Anaesthesiology) of this college has submitted a Dissertation for the study work entitled ""**Comparison of the Analgesic Efficacy of Intrathecal Isobaric Ropivacaine and Isobaric Ropivacaine with Dexmedetomidine for lower limb Orthopaedic Surgeries.**". The Study of the above individual has been approved by the Human Ethical Committee of the Chengalpattu Medical College, Chengalpattu which is forwarded herewith for further course of action.

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Last but not least, I thank all the patients for willingly submitting themselves for this study.

CONTENT

INTRODUCTION

Effective pain control is essential for care of surgical patients. Adequate post-operative pain relief must be an integral part of administration of anaesthesia. Inadequate post-operative pain relief may result in clinical and psychological changes that may increase the morbidity and mortality as well as the cost of treatment as a whole, in addition to decreasing the quality of life post-operatively.

Intrathecal local anaesthetic agent was first used by Bier. After several years of development, the technique and concept of spinal anaesthesia has improved with use of other local anaesthetics like lignocaine, bupivacaine, tetracaine. Pure isomeric compounds are now available such as Ropivacaine and Levobupivacaine with favourable clinical outcome. Ropivacaine produces shorter duration of motor block than levobupivacaine which is useful in the early mobilization of the patient and hospital discharge.

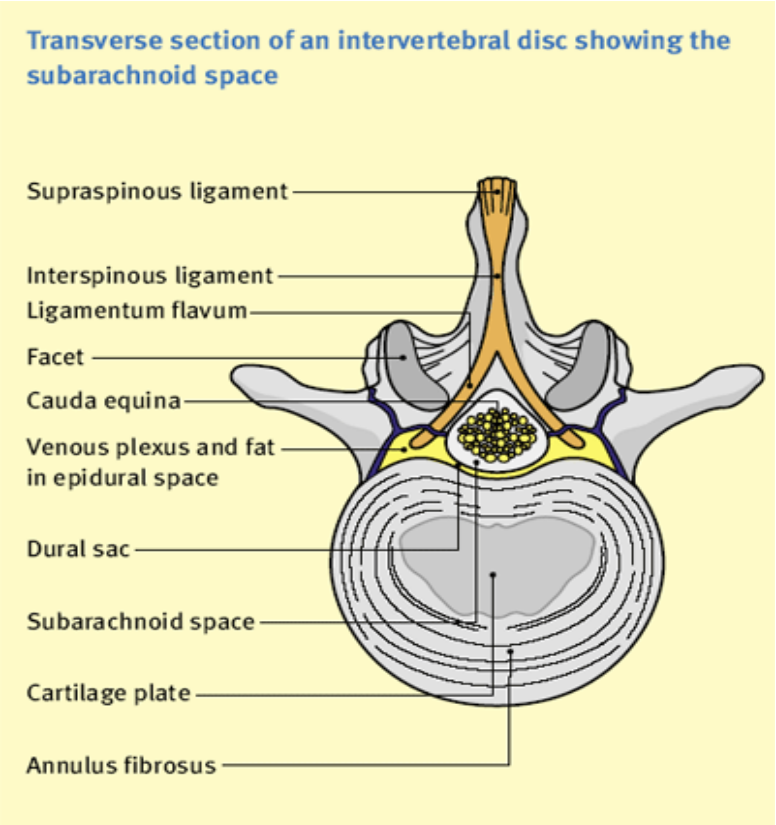
Ropivacaine is a first single enantiomer specific compound, which has a reduced risk of cardiotoxicity, neurotoxicity, and rapid recovery of motor function. Postoperative pain relief is an important issue with Ropivacaine. So, our concern is of using a drug as an adjuvant with Ropivacaine which provides better intraoperative haemodynamic condition as well as prolonged postoperative analgesia with minimal side effects.

Regionally applied opioids are effective analgesics used since middle of nineteen's century when morphine was injected perineurally The first report on intrathecal opioid anaesthesia was published in 1901 and on epidural morphine in 1979. Besides morphine various other opioids and adjuvants have been introduced to improve the efficacy of neuraxial analgesia, including NMDA antagonists (ketamine, magnesium), GABA agonists (midazolam) and adrenergic agonists (clonidine, adrenaline), COX-inhibitors (ketorolac), Ach-esterase inhibitor (neostigmine) etc.

An ideal adjuvant should provide a longer duration of analgesia and better hemodynamic stability. α-2 adrenergic agonists as an intrathecal adjuvant have excellent analgesic and minimal sedative properties [2-6]. Dexmedetomidine which is a highly selective α-2 adrenergic agonist with eight times greater affinity for receptors than clonidine. The requirements of analgesia are greatly reduced to a large extent by the use of the above mentioned adjuvants because of their unique analgesic properties. They also augment the effects of local anaesthetics by causing hyperpolarisation of nerve cells and alters the transmembrane potential and conduction of ion in the brain stem (Locus Coerulues) [11, 17, 18, 23, 24]. These are useful pharmacological agents that reduces the requirements of other analgesics and by providing better hemodynamic stability [26].

With the knowledge of pharmacological properties and drug interactions we designed a prospective randomised controlled study in a double blinded manner at our institution for the patients receiving spinal anaesthesia who underwent lower limb orthopaedic surgeries. Our aim was to compare the duration of analgesia, duration of sensory and motor blockade and incidence of side effects of intrathecal 0.75% isobaric ropivacaine with combination of 0.75% isobaric ropivacaine and dexmedetomidine.

ANATOMY OF SUBARACHNOID SPACE



Transverse secton of an intervertebral disc

Vertebral column

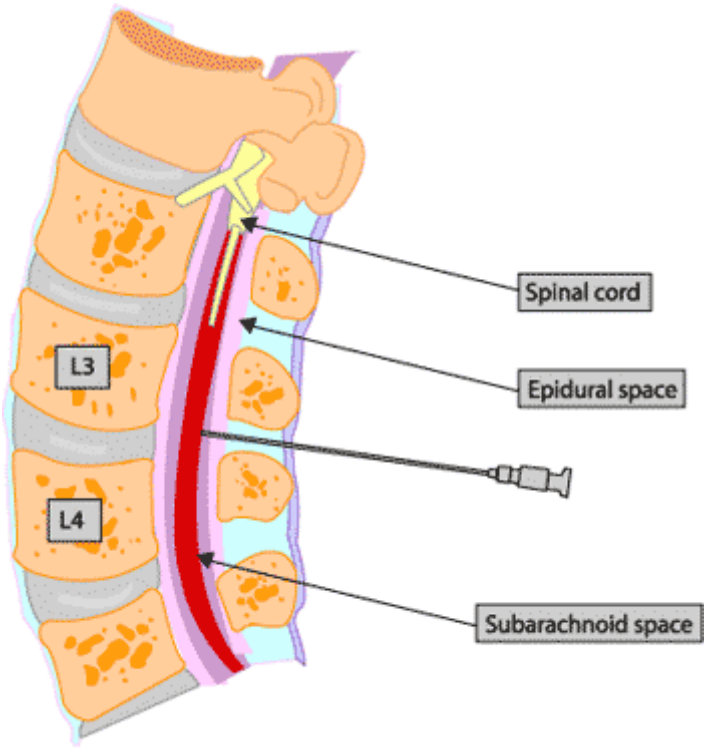
The vertebral column comprises of 33 vertebrae (7 cervical, 12 thoracic, 5 lumbar, 5 fused sacral,and 4 coccygeal), has four curves. The cervical and lumbar curves are convex anteriorly, the thoracic and sacral curves posteriorly. These curve have a significant infulence on the spread of local anaesthetics in the subarachnoid space. The vertebal column is bound together by several ligaments which give it stability and elasticity.

They are

1. Supraspinous ligament – strong fibrous cord connects the apices of spinous processes from sacrum to C7, and then extended to external occipital protruberance as the ligamentum nuchae.
2. Inter spinous ligament – thin membranous ligament connects the spinous processes, blend anteriorly with ligamentum flavum and posteriorly with supraspinous ligament.
3. Ligamentum flavum – also called as 'yellow ligament', comprises of yellow elastic fibres and connects adjacent lamina that runs from the caudal edge of the vertebra above to the cephalad edge of the lamina below.
4. Longitudial ligaments – the anterior and posterior longitudinal ligaments bind vertebral bodies together.

The spinal cord continues above with the medulla oblongata, begins at the level of the foramen magnum and ends below as the conus medullaris. It is cylindrical in shape, 45 cm in length in adults, flattened in the lumbar region. A thin thread, filum terminale is attached to the coccyx. At birth it ends at the lower border of L3 and rises to end in adult life at the lower border of L1.

There are totally 31 pairs of symmetrically arranged spinal nerve roots: Cervical 8, Thoracic 12, Lumbar 5, Sacral 5and Coccygeal 1. The cauda equina is formed by elongation of nerve roots of lumbar and sacral region before they exit from the intervertebral foramen.



Saggital section of spinal cord termination

The central nervous system is protected and supported by 3 different membrane coverings called meninges. Outer most membrane is the duramater, innermost is the piamater and arachnoid membrane is in between. The potential space between the duramater and arachnoid mater is called subdural space, and space between the arachnoid mater and pia mater is called sudarachnoid space. Extradural (epidural) space is above the duramater.

SPINAL CORD STRUCTURES

1. **Epidural (extradural) space** – between the dura mater and the periosteum. It extends from the foramen magnum to the sacral hiatus. It is a triangular space in cross-section, with two larger postero lateral and a small anterior compartments. It also extends through the spinal foramina (as the nerve roots exit) laterally. The depth of the epidural space is at 3–5 cm beneath the skin. The extradural space consists of adipose tissues, lymph vessels, arteries and venous plexus (valveless, vertebral, venous plexuses of Bateson – forming a communication between pelvic and cerebral veins)

2. **Subdural space** – a potential between the arachnoid mater and the duramater which contains thin serous fluid.

3. **Subarachnoid space** - space between the arachnoid mater and piamater contains cerebrospinal fluid (CSF), spinal nerves, a trabecular network between the two membranes, blood vessels that supply the spinal cord and lateral extensions of the piamater and dentate ligaments, which provide lateral support from spinal cord to the duramater. Although the spinal cord ends at the lower border of L1 in adults, the subarachnoid space continues to S2.

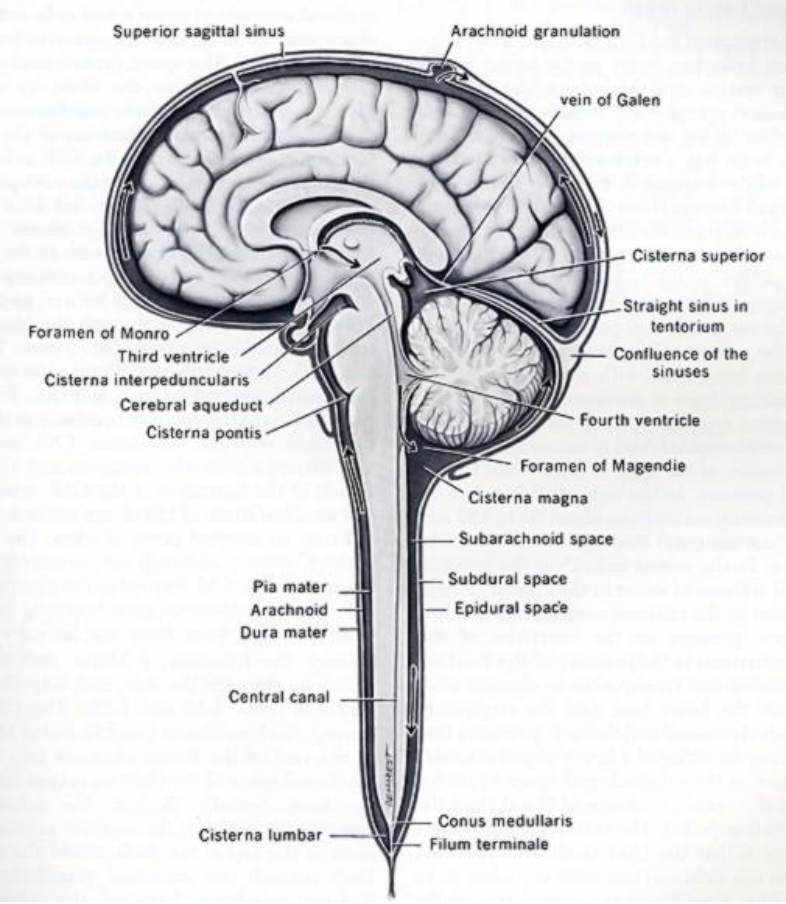
4. **Dura mater** – contains two layers of dense fibro elastic membrane in which the outer layer attaches to the foramen magnum and the

inner layer continues from the cerebral dura. The dura ends at the second sacral segment (variably L5–S3). It attaches to the coccygeal periosteum and covers the filum terminale. Anteriorly the dura is attached to the posterior longitudinal ligament and extends around the nerve roots laterally but it is free posteriorly.

5. **Arachnoid mater** – delicate, nonvascular thin membrane closely lining the duramater. Arachnoid functions as the principal barrier to drugs crossing in and out of the CSF and is estimated to account for 90% of resistance to the drug migration.

6. **Pia mater** – highly vascular connective sheath that closely covers the spinal cord. The anterior part is thickened (linea splendens) and attached to the dura laterally (ligamentum denticulatum). Posteriorly it attaches to the dura by an incomplete sheet of pia (posterior subarachnoid septum). The inferiorly it is attached to the coccyx is through filum terminale which is its continuation.

CEREBROSPINAL FLUID (CSF)



Cerebro spinal fluid circulation

Cerebrospinal fluid is an ultrafiltrate of the blood plasma, with which it is in hydrostatic and osmotic equilibrium. It is clear, colourless fluid found in the spinal and cranial subarachnoid spaces and in the ventricles of the brain.

- Volume – total volume is 150 ml and only 25 ml is present in spinal/subarachnoid space.

- Production – it is produced by the choroid plexuses of the two lateral, third and fourth ventricles. It circulates via the paired interventricular foramina (of Munro) from the two lateral ventricles to the 3rd ventricle, and to the 4th ventricle via the cerebral aqueduct. The CSF then flows through the paired lateral foramina of Lushka and the median foramen of Magendie from the 4th ventricle to the subarachnoid space
- Absorption – 80% is absorbed via the projections of arachnoid mater (arachnoid villi) in the cerebral venous sinuses. The remaining 20%is absorbed by arachnoid villi in spinal cord or by lymphatic drainage. The CSF pressure ranges from 6 to 10 cm of CSF (60 – 80mm H_2O) when lying and 20–40 cm in the lumbar area when sitting and it is gravity-dependent.
- Composition – it is composed of

  Glucose = 1.5–4.0 mmol/L,

  Sodium = 140–150 mmol/L,

  Chloride = 120–130 mmol/L,

  Bicarbonate = 25–30 mmol /L,

  Protein = 0.15–0.3 g/L,

  Cells = < 5 lymphocytes/cubic mm,

Osmolality = 280 mOsm

Specific gravity = 1006 (1003 – 1009) at temperature 37°C,

pH = 7.4,

Pco_2 = 48mmHg.

Action of local anaesthetics

Local anaesthetic prevents the sodium channel activation by binding to Na+ channels in the inactivated state. Development of the action potential is prevented by blocking the movement of Na+ into the cell. Membrane stabilization property is unique quality of the local anaesthetics where the repeated nerve stimulation will not affect the resting membrane potential.

Mechanism of action of local anaesthetics in neural blockade

In the dorsal horn neurons, local anaesthetics block both ion channels (Na+ and K+) inhibiting the generation of nociceptive electrical activity and propagation of pain (noxious) signals. Similarly it acts on the ventral horn neurons to produce the motor blockade. Centrally administered local anaesthetics produces an intense analgesic action by blocking the Ca+ channels in the spinal cord. This may lead to resistance of electrical stimulation from afferent nerves carrying pain signals. Apart from these actions local anaesthetics given through intrathecal route indirectly inhibit neurotransmitters release like substance P involved in

pain signal processing. Along with substance P, centrally given local anaesthetics blocks the presynaptic voltage-gated Ca+ channel. This leads to blockade of neurotransmitters like glutamate, substance P, calcitonin gene-related peptide (CGRP), neurokini-1 and -2 (NK1, NK2) at the presynaptic level. Therefore local anaesthetics given in spinal (intrathecal) can indirectly inhibit the transmission of pain signal.

Order of blockade in spinal

The block and recovery of sensory fibers occur in this order

Preganglionic sympathetic fibers (B-fibers) are the most sensitive to local anaesthetic

C fibers – cold sensation

A δ fibers – pin-prick

A β fibers – touch

Vibration and proprioception

Motor fibers Aα are less sensitive to local anaesthetic

Spinal anaesthesia merits and demerits

Merits of spinal anaesthesia

- Perfoming the spinal is easy
- Reliable block
- Good operating conditions for the surgeon

- Cost effective
- No airway compromise and minimal respiratory complications
- Faster recovery of gastrointestinal function post operatively
- There is reduction in deep vein thrombosis due to early ambulation

Demerits of spinal anaesthesia

- Failure due to faulty technique.
- Alterations in hemodynamic status is present.
- Resuscitation medications should be available.
- Surgery of longer duration

Factors postulated to be related to spinal anaesthetic block height

Patient factors

- Age
- Height
- Weight
- Gender
- Intra-abdominal mass due to increase in pressure
- Anatomical defects of the spinal column (kyphosis, scoliosis)
- Posture

Technique of injection

- Site of needle placement – higher the level will affect the block level .
- Needle angulation – angled cephalad – increase cephalad spread of hyperbaric solutions injected in lateral position
- Direction of bevel
- Turbulence in CSF (e.g. by barbotage)
- Rate of injection

Characteristics of spinal fluid

- Volume - Decreased CSF volume leads to higher block level and vice versa
- Pressure (cough, strain, valsalva maneuver)
- Density – hypobaric local anesthetics may not spread far. But hyperbaric solutions will result in a greater spread.

Characteristics of local anaesthetic (LA) solution

- Density of Local anaesthetic solution – L.A weight vs. CSF weight.
- Specific Gravity – density of a local anaestheic solution compared to the density of water.

- Baricity - the ratio of the density of local anaesthetic solution to density of CSF
- Amount (mass)
- Concentration - the higher the concentration, the higher the block.
- Temperature - cold solution are viscous which limits its spread. Increase in the temperature of the solution increases the spread. It is a minor consideration.

Volume –increase in volume, greater will be the spread.

Vasoconstrictors

Distribution of L.A in CSF

Factors with proven effects

- Site of injection
- Anatomic configuration of spinal column
- Patient height (only at extremes)
- Angulation of needle
- Volume of CSF (e.g. ↓ CSF vlume with ↑intra-abdominal pressure (e.g. pregnancy)
- Characteristics of L.A. solution – Density, Specific gravity, Baricity.

- Dose of L.A solution
- Volume of L.A. solution
- Position of patient during injection
- Position of patient after injection

Factors with no proven effects

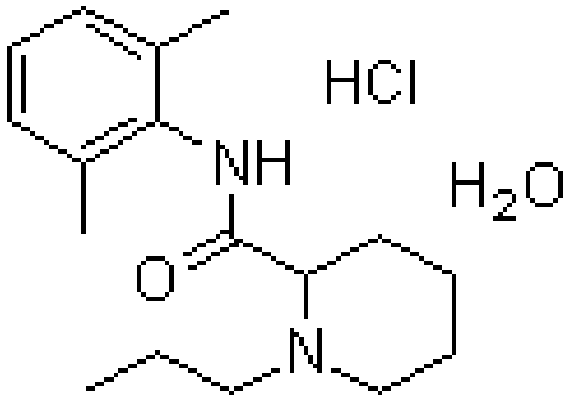
- Patient weight
- CSF composition
- Circulation of CSF
- Concentration of L.A. in solution injected
- Diffusion in CSF, independent of baricity
- Addition of vasoconstrictors
- Direction of needle bevel during injection
- Rate of injection
- Turbulence in CSF (barbotage)
- Coughing, straining, labour pain
- Age
- Gender

PHARMACOLOGY

ROPIVACAINE

Ropivacaine hydrochloride

(S)-N-(2,6-dimethylphenyl)-1-propylpiperidine-2-carboxamide hydrochloride



Stucture of Ropivacaine

Molecular Formula $C_{17}H_{26}N_2O_2 \cdot HCl \cdot H_2O$: Molecular Weight 328

Ropivacaine is amide type local anaesthetic drug with both anaesthetic and analgesic properties. At high doses it produces anaesthesia and at lower doses it produces analgesia (sensory block) due to its differential blocking effect on nerve fibres. It belongs to different local anaesthetic group, the pipecoloxylidides, which was synthesized in 1957.

Ropivacaine, a local anaesthetic with increased duration of action, which is similar in structure to Bupivacaine. In contrast to Bupivacaine, Ropivacaine a pure S (-) enantiomer, has reduced toxicity and at the same time improved sensory and motor block. It acts on different ion channels like sodium, potassium, and calcium with different affinity that leads to greater reduction in neuronal toxicity and cardiovascular side effects. Ropivacaine is derived as a pure form of S (-) enantiomer from propivacaine, the parent molecule with chiral property. It is a pipecoloxylidides group of local anaesthetics with the piperidine nitrogen atom having a propyl group.

Ropivacaine causes reversible blockade of impulse propagation by inhibition of sodium ion influx in nerve fibres. It inhibits the potassium channels in dose-dependent manner. Because of less lipid solubility than bupivacaine, it minimally penetrates the large myelinated Aβ motor fibres, this explains its more specific action on the pain-transmission through Aδ and C nerves rather than Aβ fibres (motor function).

Ropivacaine has fewer propensities for cardiac and CNS adverse effects because of its stereo selective property. It has similar efficacy of levo bupivacaine and Bupivacaine in blocking peripheral nerve. When given neuraxially (epidural or intrathecal) it is less potent than bupivacaine. It is associated with incidence of lower grade motor blockade when compared to bupivacaine. Because of its lower grade

motor blockade, reduced potential for CNS and cardiac adverse effects it is new agent of choice for regional anaesthesia.

PHARMACOKINETICS[30]

The plasma concentration varies depends on the dose, route of administration and injection site vascularity. Ropivacaine follows linear pharmacokinetics Cmax is proportional to the dose. When given extradural its absorption is biphasic (t1/2 is 4mins and 4 hrs) and complete. Elimination of ropivacaine is mainly depends on absorption which is a rate limiting step. Epidurally given drug has longer t1/2 compared to intravenous route. The terminal half life of ropivacaine is 1.8hrs after IV route.

Ropivacaine is highly protein bound particularly to α1-acid glycoprotein and only 6% present as unbound fraction. It crosses easily through the placenta and degree of plasma protein binding in fetus is less compared to mother.

METABOLISM

It is metabolized mainly by aromatic hydroxylation particularly in liver. If given IV, large doses are excreted via urine for about 86% out of which only 1% is unchanged fragment. The main metabolite is 3-hydroy-ropivacaine is excreted after conjugation. Other metabolites like 4-hydroxy-ropivacaine,the N-dealkylated metabolite 2', 6'-

ipecoloxylidide and 4-hydroxy dealkylated are present only in minimal quantities in plasma. Similar kind of kinetics is present in children more than 1 year. The PPX (2', 6'-pipecoloxylidide) has longer t1/2 and lower clearance after infusion through epidural.

- Clearance – unbound ropivacaine – 13.94L/h/Kg
- Clearance – Total ropivacaine – 0.555L/h/Kg
- Volume of distribution – 65.57L/min
- Terminal t1/2 of ropivacaine - 3.3hrs
- Terminal t1/2 of PPX – 17.8 hrs

CONTRAINDICATIONS

- Hypersensitivity to any amide type local anaesthetic.
- Not recommended where faster onset of surgical anaesthesia is required.
- Intravenous regional anaesthesia.
- Paracervical block in obstetric anaesthesia.
- Hypovolemia.
- Premature children.

PRECAUTIONS

- Accidental intravenous administration results in cardiac arrest and convulsions.
- Retrobulbar block because of less clinical evidence.
- Patient with poor general condition
- Liver disease.
- Kidney dysfunction.
- Acute porphyria

DRUG INTERACTIONS

- Duration and intensity of block will not be altered by adding adrenaline.
- Additive effects with other local anaesthetics.
- Other anti-arrhythmic drugs.
- Used with potent enzyme inhibitors like fluvoxamine, verapamil will prolong the half life.
- Used with ketaconazole reduces the plasma clearance by 15 %.

INDICATIONS

- Epidural block for surgical anaesthesia for abdominal surgeries, pelvic, lumbar and lower limb, Caesarean section.
- Paediatric caudal block
- Spinal anaesthesia.

- Nerve blocks.
- Field and filtration blocks.

DOSAGE AND ADMINISTRATION

- Caudal – 1mg/kg, 0.2% or 2mg/ml produces a level below T12.
- Epidural block with 6-14 ml of 0.2% ropivacaine provide adequate analgesia.
- Spinal – 2-3ml of 0.75 %(7.5mg/ml) with doses between 15-22.5mg results in sensory block upto T4 or T5

Surgical anaesthesia	**Concentration mg/ml**	**Volume (ml)**	**Dose (mg)**	**Onset (minutes)**	**Duration (hours)**
Lumbar epidural, pelvic, and lower limb surgeries	5.0 7.5	15-30 15-25	75-150 113-188	15-30 10-20	2-4 3-5
Nerve blocks	5.0 7.5	35-50 10-40	175-250 75-300	15-30 10-25	5-8 6-10
Field block	5.0 7.7	1-40 1-30	5-300 7.5-225	1-15 1-15	2-6 2-6

PREGNANCY AND LACTATION

No well controlled studies in pregnant and nursing mothers.

ADVERSE EFFECTS

- Hypersensitivity reactions
- Main effects-Hypotension, bradycardia, vomiting, urinary retention, raised body temperature, rigors, back pain.
- Less common effects – CNS toxicity, cardiac toxicity
- Spinal cord dysfunction such as anterior spinal artery syndrome, arachnoiditis, cauda equina syndrome.

Other effects

It has some antibacterial properties and some action on inhibition of platelet aggregation

INTRATHECAL ADMINISTRATION

Ropivacaine is less potent than bupivacaine in equal volume of doses of similar concentration . Hyperbaric solutions has faster onset and more reliable block with good recovery.because of the variability in spread and duration of the block hyperbaric Ropivacaine solutions are not available commercially. When administered with opioids ropivacaine not only reduces the total dose of local anaesthetic but also causes significant

prolongation in the duration of complete and effective analgesia without increase the duration of motor block.[3]

A research on lower limb surgeries with 15 mg of Ropivacaine was found to be equipotent with 10mg of Bupivacaine with respect to sensory block but not for the motor block which was significantly of shorter duration. The potency of Ropivacaine relative to Bupivacaine is 2/3rd with regard to sensory block and ½ with regard to motor block(4).

PHARMACOLOGY OF α-2 AGONISTS

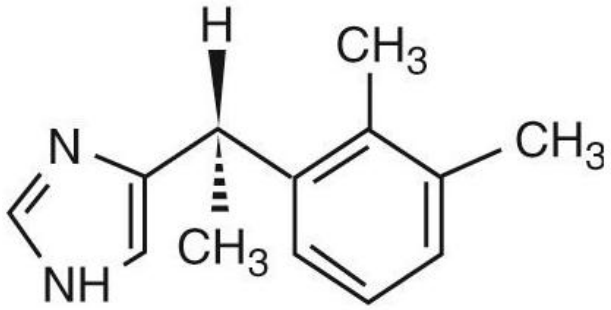
HISTORY

Historically α2-agonists have been used in treating hypertensive patients and for withdrawl symptoms in alcohol and drug abusers. α2-agonists provide sedation, antianxiety, hypnosis, analgesia and also inhibit sympathetic system.

Dexmedetomidine is more selective α_2 agonist with 1600 greater selectivity for α_2 receptor compared with α_1 receptor. It was introduced in 1999 as a short term sedative agent in ICU for adult patients on mechanical ventilator. But now it is widely used as sedative, adjunct analgesia for various diagnostic procedures.

PHYSIOCHEMICAL CHARACTERISTICS[29]

Dexmedetomidine is the d-enantiomer of medetomidine. It belongs to imidazole subgroup of α_2 agonist. The receptor specificity ratio 1600:1(α_2: α_1). It is freely soluble in water.



Structure of Dexmedetomidine

Physiological functions of α 2 receptors

α 2a –presynaptic feedback inhibition of norepinephrine release

Hypotension

Analgesia

Sedation

Inhibition of epileptic seizures

α 2b –hypertension

Placental angiogenesis

Analgesic effect of nitrous oide

α 2c –feedback inhibition of adrenal catecholamine release

Analgesic effect of moxonidine

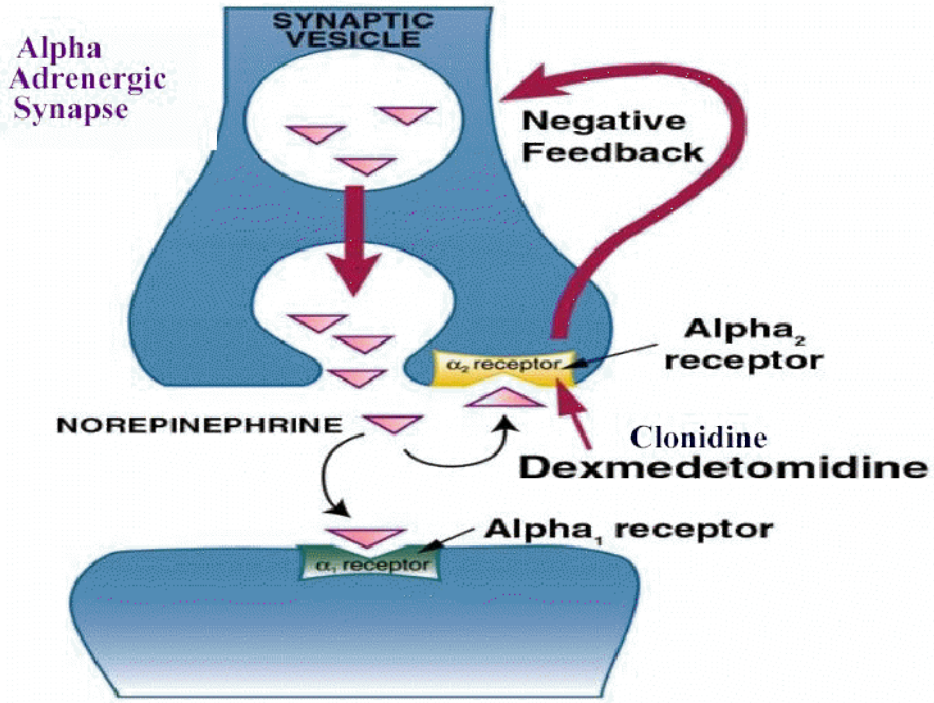
Modulation of behaviour

Mechanism of action

1. Activate inhibitory action of G proteins leading to decrease in cyclic AMP.
2. Activate G proteins which directly act on membrane bound ion channels, particularly potassium channels.
3. Activate Nitric Oxide, cyclic GMP pathway by inhibiting the release of noradrenaline within neuronal tissue.

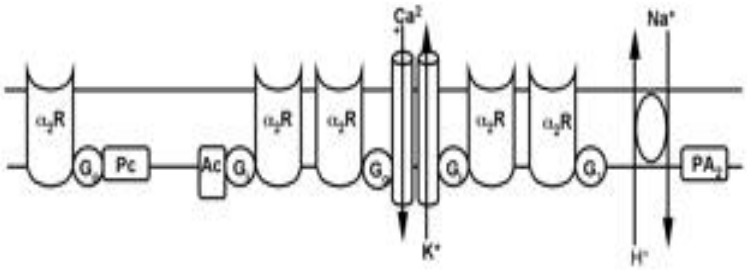
In the dorsal motor complex of medulla it causes hypertension and bradycardia. Action on locus coeruleus leads to sedation and analgesia.

There is high density of receptors in the vagus nerve, intermediolateral column and the substantia gelatinosa, dorsal horn of the spinal cord and Primary sensory neurons.



α_2 adrenoceptors

$\alpha_2$receptors are G-protein-coupled receptors in the transmembrane region of the central and peripheral nervous system particularly at autonomic ganglion of presynaptic and post-synaptic region. Nor epinephrine (Endogenous agonists) and clonidine (exogenous agonists) acts on these receptors inhibit the enzymes adenylyl cyclase and phospholipase C resulting in the inhibition of calcium ion (Ca^+) entry and facilitation of opening potassium ion (K^+) channels outwards that results in hyperpolarization.



Binding of agonists at the α_2-adrenoceptor results in coupling with G-proteins due to conformational change in receptor protein.

The α_2-adrenoceptor (α_2R)

- Inhibits adenylyl cyclase (Ac) through the inhibitory G_i protein
- Causes outward opening of K^+ channel via G_i protein, which results in hyperpolarisation
- Inhibits Ca^{2+} translocation via G_o protein
- Modulates Phospholipase C (Pc) via G_o protein
- Is coupled to an exchange of H^+ and Na^+ ions via an undetermined G protein ($G_?$)

Structure of α_2-adrenoceptors

Possible mechanism of action of α_2-adrenoceptors

Pre-synaptic activation of α_2-adrenergic receptors in sympathetic nerve endings and noradrenergic neurons inhibit norepinephrine release. In Central nervous system it leads to inhibition of sympathetic activity, resulting in hypotension, bradycardia and sedation. However, at higher doses it produces hypertension through receptor activation present on smooth muscle cells of the resistance vessels. The hypnosis is mediated through α_2-receptors of the locus coeruleus, analgesia is mediated by α_2-adrenoceptors of spinal cord. Imidazole ring of the α_2-agonist drugs may interact with imidazoline receptors. Clonidine and Dexmedetomidine (Dex) belong to imidazoline compounds.

Pharmacokinetics

Dexmedetomidine is rapidly distributed and extensively metabolized in liver and excreted in urine and feces. It undergoes conjugation (41%), n-methylation (21%), or hydroxylation followed by conjugation. It is 94% protein bound to serum albumin and α_1-glycoprotein, hence has a volume distribution of approximately 200 litres and its concentration ratio between whole blood and plasma is 0.66. It displays nonlinear pharmacokinetics and best described by three compartment model. The elimination half life is 2 to 3 hours, with a context sensitive half life of 4 mins after 10 mins of infusion to 250 mins after an 8 hour infusion.

Dexmedetomidine after IV exhibits the following pharmacokinetics: a rapid distribution phase with half-life (t½) of 6 minutes; elimination t½ of about 2 hours; and volume of distribution at steady-state (Vss) of around 118 litres. Clearance is about 39 L/h for a 72 kg person.

Distribution

Dexmedetomidine bind to plasma protiens of 94% which is constant for different concentration in plasma which is similar for both sexes. Patients with decompensated liver disease have decreased binding to plasma proteins.

Dexmedetomidine hydrochloride displaces, fentanyl, ketorolac, digoxin, theophylline and lidocaine from protein binding in laboratory settings. In vitro the displacement of the drugs like ibuprofen, phenytoin, warfarin, propranolol, digoxin and theophyllin are not significant.

Metabolism

There is almost complete biotransformation of dexmedetomidine with very little unchanged amount is excreted in urine and feces. Biotransformation occurs via both direct glucuronidation as well as cytochrome P450 mediated metabolism.

The major metabolic pathways are

1. Direct N-glucuronidation to inactive metabolites;
2. Aliphatic hydroxylation (mediated primarily by CYP2A6) to 3-hydroxy-dexmedetomidine, the glucuronide of 3-hydroxy-dexmedetomidine, and 3-carboxydexmedetomidine
3. N methylation of dexmedetomidine to generate 3-hydroxy N-methyl-dexmedetomidine, 3-carboxy N-methyl-dexmedetomidine, and dexmedetomidine-N-methyl O-glucuronide.

Elimination

The dexmedetomidine has terminal elimination half-life (t½) of approximately 2 hours and clearance estimated to be approximately 39 L/h

Age and Gender

Dexmedetomidine hydrochloride does not show any variation in pharmacokinetics in both the sexes and in all age groups.

Pediatrics

The researches are minimal in children regarding the pharmacokinetics.

Hepatic Impairment

Hepatic clearance values are lower depends on degree of hepatic derangement. It is necessary to reduce the dose in patients with hepatic derangement depending on variations in liver function test.

Renal Impairment

Dexmedetomidine hydrochloride pharmacokinetics (Cmax, Tmax, AUC, t½, CL, andV_S) do not vary in patients with severe renal impairment (creatinine clearance: < 30 mL/min) compared to healthy subjects. Since the metabolites are excreted in urine they may accumulate on long term infusion.

Drug Interactions

No evidence of cytochrome P450 mediated drug interactions that are likely to be of clinical relevance. Co-administration with anaesthestic, sedatives, hypnotics or opioids may lead to enhancement of their effect. These drugs may require reduction of dose. It may have additive effect with vasodilator and negative chronotrophic agents. Midaolam and propofol co administration may lead to increased incidence of bradycardia and hypotension hence require more caution.

Pregnancy,Labour and Lactation

There were no adequate and well controlled trials. Hence should used with caution.

Adverse effects

Most frequently observed side effects are hypo or hypertension, dry mouth, bradycardia and nausea. Other side effects are fever, arrhythmias, AV block, extra systoles, pulmonary oedema, dizziness, headache etc

Alpha 2 antagonist

Atipamezole

Atipamezole, a selective a2-adrenoceptor antagonist readily reverses the sedative properties of Dexmedetomidine. Intravenous atipamezole reverses the sedation and sympatholysis in dose-dependent manner. Because of the similar elimination half-lives of both agonist and the antagonist, the clinical effect of Dexmedetomidine after reversal by atipamezole is very minimal. Therefore the dexmedetomidine provides hypnosis and sedation in titrated doses and reversed easily by atipamezole.

REVIEW OF LITERATURE

1. **Kallio H et al**[11] (2004) had conducted a prospective randomized double-blinded study in 90 patients who had undergone lower limb surgeries. They had received 2ml of 1% ropivacaine (20mg), 0.75% ropivacaine (15mg), or 0.5% bupivacaine (10mg) in spinal anesthesia. They assessed the motor block with the modified Bromage scale, and pinprick to assess the sensory block. Ropivacaine 15 mg had a shorter duration of motor block (150 mins) than bupivacaine 10 mg (210 min; P = 0.005), but they did not differ significantly in the median duration of motor block at T10 (140 min) for both groups. There was a significantly longer duration of sensory block at T10 with ropivacaine 20 mg (170 min) than with bupivacaine 10 mg (140 min; P = 0.005), but they did not differ significantly in the median recovery from sensory block (210 min). They concluded that the duration of sensory block of ropivacaine was only two thirds and the motor block duration was half when compared with bupivacaine, based on the duration-per-mg of the local anesthetic agent.

2. **Antonio Mauro Vieira et al** [3] (2004) conducted a study to evaluate the analgesia and sedation promoted by clonidine or dexmedetomidine associated to epidural ropivacaine in the postoperative period of subcostal cholecystectomy. Clonidine and

dexmedetomidine are α-2-adrenergic agonists with analgesic proprieties which potentiate local anaesthetic effects when epidurally administered. Forty patients of both gender were participated in this randomized double-blind study, aged 18 to 50 years, weighing 50 to 100 kg, physical status ASA I or II, submitted to subcostal cholecystectomy. The subjects were distributed in two groups: Clonidine (CG) received clonidine (1 mL = 150 μg) associated to 0.75% epidural ropivacaine (20 mL); Dexmedetomidine (DG) received dexmedetomidine (2 μg/kg) associated to 0.75% epidural ropivacaine (20 mL). Analgesia and sedation were evaluated 2, 6 and 24 hours after anesthetic recovery. Both groups presented some grade of sedation at 2 and 6 hours, with statistically significant difference between the two moments for the dexmedetomidine group. There has been analgesia in both groups, especially at 2 and 6hours. There has been statistically significant difference among periods of 2, 6 and 24 hours in the dexmedetomidine group; in the clonidine group, this statistically significant difference was observed between the periods of 2 and 6 hours and between 2 and 24 hours. To conclude that the association of clonidine or dexmedetomidine to 0.75% ropivacaine induces analgesia and sedation in 2 and 6 hours after anaesthetic recovery in patients submitted to subcostal cholecystectomy and that clonidine promotes more prolonged analgesia.

3. **Kanazi GE et al** [19] (2006) in a prospective double-blind study in 60 patients who were randomly allocated into group B (bupivacaine 12mg), group C (bupivacaine 12mg + 30 ug of clonidine and group D (12 mg of bupivacaine + 3ug of Dexmedetomidine) underwent transurethral prostatic resection and bladder tumour resection under spinal anaesthesia. They had compared the onset and duration of sensory block and motor block, heart rate and blood pressure changes and sedation. They had found longer sensory and motor regression in patients in groups D and C which was significant and significantly shorter onset time of motor block than patients in group B. The mean time regression of sensory level to the S1 segment was 190 +/- 48 minutes in group B, 272 +/- 38 minutes in group C and 303 +/- 75 minutes in group D ($P < 0.001$). The regression time of Bromage 0 was 163 +/- 47 minutes in group B, 216 +/- 35 minutes in group C and 250 +/- 76 minutes in group D ($P < 0.001$). Patients belong to groups D and C did not show significant difference in the onset and regression times. There was no significant difference in the hemodynamic variability and level of sedation in all the three groups during intra-operative and post-operative period. They concluded that Dexmedetomidine (3ug) or clonidine (30ug), given with intrathecal bupivacaine, produces a longer duration of the motor block and sensory block, stable hemodynamics and minimal sedation.

4. **Al-Mustafa MM et al** [21] (2009) assigned 60 patients and studied the effect of adding dexmedetomidine to bupivacaine for neuraxial anesthesia. They were randomly divided into 3 groups, group N (bupivacaine 12.5mg with normal saline), group D5 (Dexmedetomidine 5 ug), or group D10 (Dexmedetomidine 10 ug). The onset time to reach dermatome T10 level and modified Bromage 3 grading of motor blockade, and the time to S1 segment regression and modified Bromage 0 grade of motor blockade were recorded. The mean time to attain the sensory level of T10 dermatome was 9.5 +/- 3.0 minutes in group N, 6.3 +/- 2.7 minutes in group D5 and 4.7 +/- 2.0 minutes in D10 group. The mean time to reach complete motor blockade (modified Bromage 3 scale) was 18.0 +/- 3.3 minutes in group N, 13.0+/-3.4 mins in D5 and 10.4 +/- 3.4 mins in group D10. The regression time to reach dermatome S1 level was 165.5 +/- 32.9 mins in group N, 277.1 +/- 23.2 mins in group D5, and 338.9 +/- 44.8 mins in group D10. The regression to Bromage 0 was 140.1 +/- 32.3 minutes in group N, 246.4 +/- 25.7 minutes in D5 and 302.9 +/- 36.7 minutes in D10. The onset and regression of both sensory and motor block were statistically significant ($p<0.001$). They had concluded that Dexmedetomidine prolongs the onset and regression time of both sensory and motor block in a dose dependent manner when given as an intrathecal adjuvant to bupivacaine.

5. **Mausumi Neogi et al** [14] (2010) had conducted a prospective randamized study to assess and compare the analgesic efficacy of clonidine and dexmedetomidine used as adjuvant to ropivacaine for paediatric patients received caudal analgesia. Seventy five patients who underwent elective inguinal herniotomy were divided randomly into three following groups. Group R (1 ml/kg of 0.25% ropivacaine), Group C (1ml/kg of 0.25% ropivacaine and 1ml/kg clonidine), Group D (1 ml/kg of 0.25% ropivacaine and 1 μg/kg dexmedetomidine). CRIES scale was used to asseess the analgesia during postoperative period. The duration of analgesia was 6.32±0.46 hrs in group R, 13.17±0.68 hrs in group C and 15.26±0.86 hrs in group D. The duration of analgesia was significantly prolonged in both the groups C and D in comparison to group R. The three groups did not differ significantly in the incidences of side effects. They concluded that both clonidine and dexmedetomidine when given caudally with ropivacaine administered significantly increase the duration of analgesia.

6. **Gupta R et al** [1] (2011) conducted a randomised double blind trial in **s**ixty patients to study the efficacy and safety of intrathecal dexmedetomidine added to ropivacaine by giving either 3 ml of 0.75% isobaric ropivacaine + 0.5 ml normal saline (Group R) or 3 ml of 0.75% isobaric ropivacaine + 5 μg dexmedetomidine in 0.5 ml of normal saline (Group D).They obtained the following results.

The mean time of sensory regression to S2 was 468.3±36.78 minutes in group D and 239.33±16.8 minutes in group R. Duration of analgesia (time to requirement of first rescue analgesic) was significantly prolonged in group D (478.4±20.9 minutes) as compared to group R (241.67±21.67 minutes). The maximum score for pain assessed by visual analogue scale was less in group D (4.4±1.4) as compared to group R (6.8±2.2). They had concluded that the addition of dexmedetomidine to ropivacaine intrathecally produces a prolonged duration of analgesia, sensory and motor blockade.

7. **Gupta R et al** [20] (2011) had studied 60 patients who underwent surgeries of lower abdomen. They were divided into two equal groups and received spinal anaesthesia with either 12.5 mg of bupivacaine with 5μg of dexmedetomidine (group D) or 12.5 mg of bupivacaine with 25μg of fentanyl (group F). They had studied the onset and duration of sensory and motor block, changes in heart rate and blood pressure, duration of analgesia and side effects in both the groups. They had found that the patients in group (D) had a longer duration of sensory block and motor block than in group (F) which was statistically significant. The mean time regression to S1 segment regression was 476±23 min in group D and 187±12 min in group F which was significant. The duration of motor block

was 421±21 min in group D compared to group F which was 149±18 min. They had concluded that the dexmedetomidine given via spinal is associated with longer duration of sensory and motor block, stable hemodynamics and reduced analgesic usage in first 24 fours.

8. **Eid HEA et al**[22] (2011) investigated 48 adult patients who underwent reconstruction of anterior cruciate ligament and were randomly divided into three groups. Each group of patient has recieved 3.5 ml volume of drug that consisted of 3 ml hyperbaric solution of 0.5% bupivacaine and 0.5 ml of either 10 μg dexmedetomidine (Group D1), 15μg dexmedetomidine (D2) or normal saline (Group B). Heart rate, blood pressure, duration of sensory and motor block, pain score, sedation level and incidence of side effects were recorded during intraoperative and upto 24 hours after intrathecal administration. They found out that there were statistically significant differences in two segment regression times, regression time to S1 segment, regression to modified Bromage 0 and time to first demand analgesia. There was a significant decrease in pain scores postoperatively. The effects were more in group D2 than in group D1. Group D2 patients had more sedation scores and lesser analgesic requirements in the postoperative period than Group D1 or B. There was no statistical difference in hemodynamic variability. They had concluded that

the dexmedetomidine in different doses of 10 μg and 15 μg prolong the anesthetic and analgesic effects significantly with spinal bupivacaine in a dose-dependent manner. A 15μg dose might have significant effects for complex lower limb surgical procedures

9. **Shukla et al** [16] (2011) conducted a prospective randomized double-blind study in 90 patients who underwent lower abdominal surgeries. They were randomly allocated in three equal groups and received 15 mg of spinal hyperbaric bupivacaine with 0.1 ml (10μg) of dexmedetomidine (group D) or 15 mg hyperbaric bupivacaine with 0.1 ml (50 mg) magnesium sulfate (group M) or 15mg hyperbaric bupivacaine with 0.1 ml normal saline (group C) as control. They had evaluated the onset and duration of sensory and motor block, duration of analgesia and side effects of dexmedetomidine and magnesium sulfate given with 0.5% bupivacaine for spinal anesthesia. They had found that the quicker onset of anesthesia and longer duration of analgesia in the dexmedetomidine group (D). They also showed that in group (M) the onset of block was delayed but significantly prolonged duration compared to control group (C), but to a lesser in group (D). The groups were similar with respect to hemodynamic changes and no significant side-effects in both the groups.

10. **Vijay.G.Anand et.al**[15] (2011)conducted a study to compare the effects of caudal dexmedetomidine combined with ropivacaine to provide post operative analgesia in children. The study was conducted in 60 children who had undergone lower abdominal surgeries. They were allocated into 2 groups of 30 each. Group RD received 0.25% ropivacaine 1 ml/kg with dexmedetomidine 2µg/kg (made up to 0.5ml) and group R received 0.25% ropivacaine 1ml/kg + 0.5 ml normal saline. Induction was done with 50%$N_2O$and 8% sevoflurane in O_2 in spontaneous ventilation and then LMA was inserted .After that caudal block was performed and the study drug was given as mentioned above. The duration of post operative analgesia was recorded and median of 5.5 hrs in Group R compared with 14.5 hours in Group RD, with a p value of <0.001.Group R patients achieved and statistically significant higher FLACC score compared to RD patients. The mean sedation score, emergence behaviour score, mean emergence time was statistically highly significant (<0.001).The peri operative hemodynamics were stable in both groups. To conclude caudal dexmedetomidine (2µg/kg) with 0.25% ropivacaine 2ml/kg for paediatric lower abdominal surgeries achieved significant post operative pain relief that resulted in a better quality of sleep and prolonged duration of arousable sedation.

AIM OF THE STUDY

Comparison of duration of analgesia, duration of sensory and motor blockade and incidence of side effects of intrathecal isobaric 0.75% Ropivacaine and combination of intrathecal isobaric 0.75% Ropivacaine and Dexmedetomidine for lower limb orthopaedic surgeries

MATERIALS AND METHODS

The study was conducted at Chengalpattu Medical College between 2011-2012 with ethical committee approval from the institution.100 patients were randomly selected based on inclusion criteria and allocated into two equal groups

Study design: A prospective randomized double-blinded study.

Sample size: 100 patients were selected and allocated in two groups randomly.

Inclusion criteria

- ASAI & II
- Either sex
- 18-60 years for lower limb Orthopaedic surgery

Exclusion criteria:

- Patient refusal
- Patients who had contraindications for spinal anaesthesia
- Allergy to local anaesthetics
- Cardiac disease
- Hypertension

Preoperative preparation

Patients, age, body weight and baseline vital parameters were recorded. History regarding previous anaesthesia, surgery and significant other co morbid illness, medications and allergy was recorded. Complete physical examination and airway assessment were done.

In the preoperative period all patients were instructed about the benefits of spinal anaesthesia and 10-point visual analogue scale. And we obtained informed consent from all the study group patients.

Premedication

All patients were premedicated with T.Ondansetron and T.Ranitidine 150 mg at 6 am on the day of surgery. They also received T.Diazepam0.2mg/kg orally night before surgery and on day of surgery. Patients were preloaded with ringer lactate at 15ml/kg.

Materials Used

- Spinal needle (Quincke) 23 or 25G
- 5 Ml syringe
- 4 ml ampoule of 0.75% isobaric Ropivacaine (Preservative free)
- 1 ml ampoule of 100 ug Dexmedetomidine.

Monitoring and intravenous access

Continuous ECG and SpO_2, automated intermittent non invasive blood pressure monitoring done. Intravenous access was done using 16 or 18 Gauge venflon and intravenous crystalloid was started.

Procedure

Preoperative heart rate, SpO_2, blood pressure was obtained. Under strict aseptic precautions with the patients in sitting position subarachnoid block was performed using 23-25G Quincke needle at L3-4, orL4-5space. Patients were divided into two following groups randomly by lot method.

Group R: Received 3ml volume of 0.75% isobaric ropivacaine and 0.5ml normal saline.

Group D: Received 3ml volume of 0.75% isobaric ropivacaine and 5µg dexmedetomidine in 0.5ml normal saline.

The consultant who prepared the drug combination did not participate in the monitoring or assessment of the patient. The person who perfomed the spinal anaesthesia as well as monitoring was blinded to the groups the patient belongs to. Injections were given over approximately 10 to 15 seconds. Immediately after completion of the block, patients were made to the supine position.

Heart rate, SpO_2, blood pressure were recorded every 5min for 30 min following subarachnoid block and every 10min there after till surgery finishes. Oxygen 4L/min was administrated through a face mask. Hypotension defined as a decrease in mean arterial pressure more than 30% from baseline or less than 80 mm Hg was treated with incremental intravenous (IV) doses of ephedrine 6 mg and boluses of IV fluid as required. The incidence of adverse effects such as nausea, vomiting, shivering, itching, pruritus, respiratory depression, sedation and hypotension was recorded.

Sensory level was assessed using loss of pinprick sensation and dermatomal level was tested every 2 minutes until the highest level had stabilised for 4 consecutive tests. Testing was done every 10 minutes until the point of two segment regression of the sensory level. Testing was performed by an anaesthetist who was blinded to the patient group. Testing was continued every 20 minutes until the recovery of S1 dermatome.

Motor block was assessed using modified Bromage scale

- 0 - no motor block,
- 1 - Inability to lift the extended legs, but can bend knees and feet
- 2 - Inability to lift extended leg and move knee, but can move feet
- 3 – full motor block of the limb

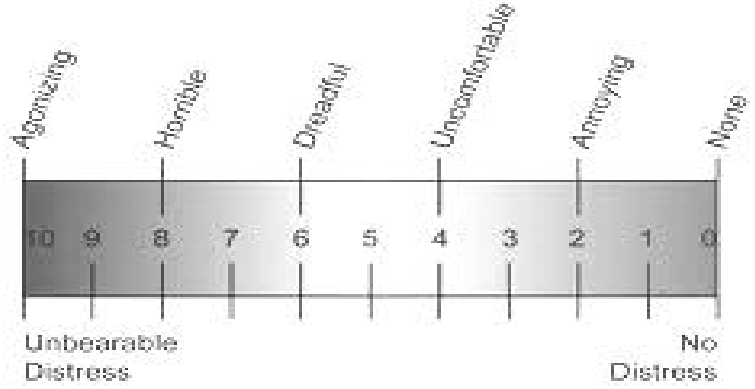
The surgeon and the observing anaesthetist were blinded to the patient groups. Data regarding the highest dermatomal level of sensory blockade, the time to reach the highest sensory level from the time of injection, time to S1 sensory regression and incidence of side effects were collected.

Four-point verbal rating scale was used to assess the sedation

(1 = no sedation, 2=light sedation, 3=somnolence,

4= deep sedation).

Assessment of Pain using visual analogue score



The pain was assessed using visual analogue scale was used to assess rating from 0 to 10 during intraoperative period

Post operative Monitoring

Postoperatively, pain scores were recorded by using VAS between 0 and 10 (0 = no pain, 10 = the most severe pain), initially every 1 hour for 2 hours, then every 2 hours for next 8 hours and then after every 4

hours till 24 hours. Injection Diclofenac 75 mg intramuscular was given as rescue analgesia when VAS ≥4.

Recording of adverse effects

During the intraoperative and postoperative period, adverse events like nausea, vomiting, shivering, dry mouth were noted. Nausea,vomiting were managed with 4mg of ondansetron intravenously. Shivering was treated with Inj. Tramadol 100mg slow IV.

OBSERVATIONS AND RESULTS

The following observations were made and datas were collected

- Heart Rate, Blood pressure, SpO_2 every 5 minutes until 1 hour and at every 15 minutes for next one hour and then every 60 minutes for next 22 hours. Hypotension (defined as fall in systolic arterial pressure less than 90mmHg) was managed with inj.Ephedrine 6mg and bradycardia (pulse rate <50 /min) was treated with 0.3mg of inj.Atropine.
- Time to achieve maximum sensory block in minutes
- Time to two segment regression from highest sensory level in minutes
- Duration of motor blockade in minutes
- Duration of analgesia in minutes
- Highest VAS score
- Incidence of side effects

STATISTICAL ANALYSIS

Data were analysed using INSTAT 3 (Graph Pad Software, California, USA).Two sided independent student' s *t* tests to analyse continuous data, Fisher's exact test and chi-square test for categorical data were used. $P<0.05$ was considered as statistically significant.

RESULTS

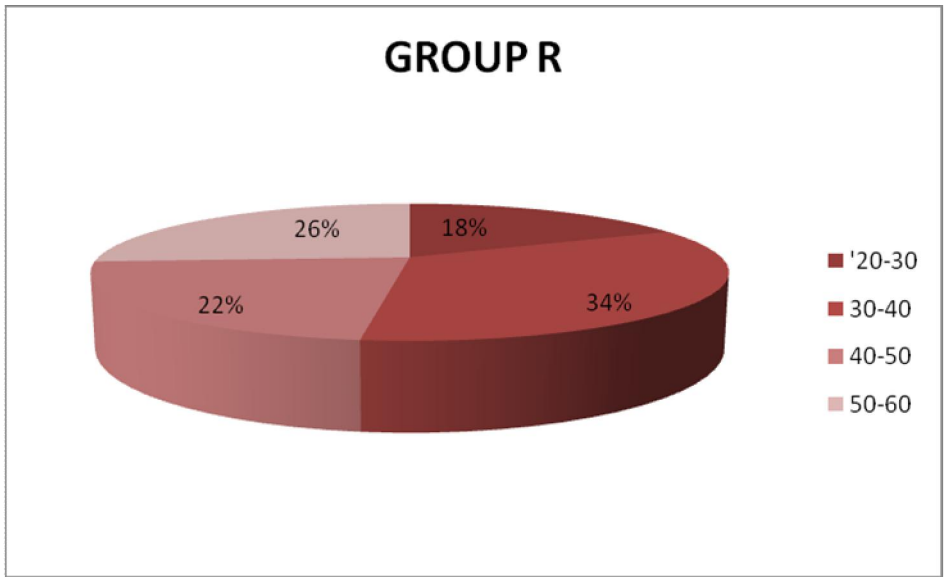
DEMOGRAPHIC DATA

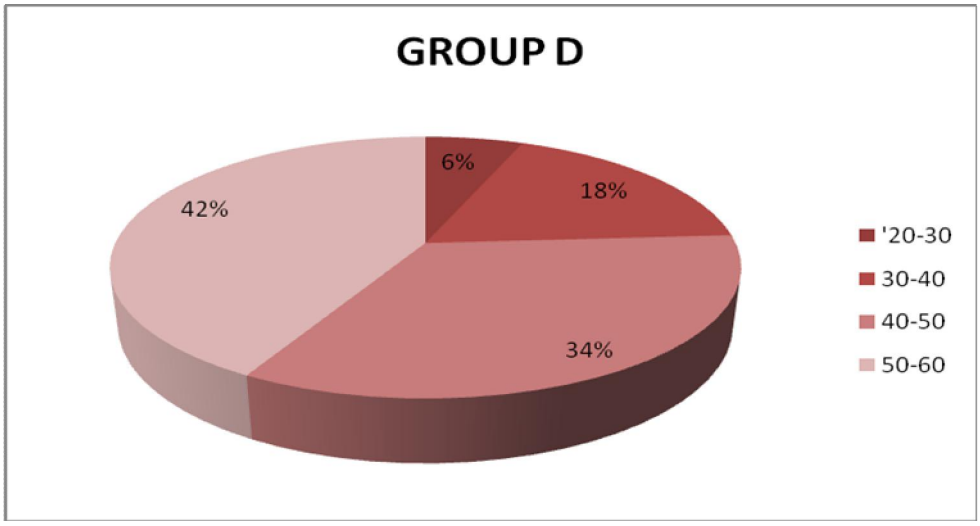
The two groups were comparable with respect to their age, weight, sex and ASA Physical status. There was no statistically significant difference among two groups in demographic profile.

AGE (student's t test)

	No. of cases	**Mean ± S.D**	**p value**
Group R	50	41.92± 11.65	0.0032
Group D	50	48.98±8.816	

The mean age in years was 41.92± 13.03 in Group R and 48.98± 9.68 in Group D. There was statistically significant difference between two groups (P<0.05).

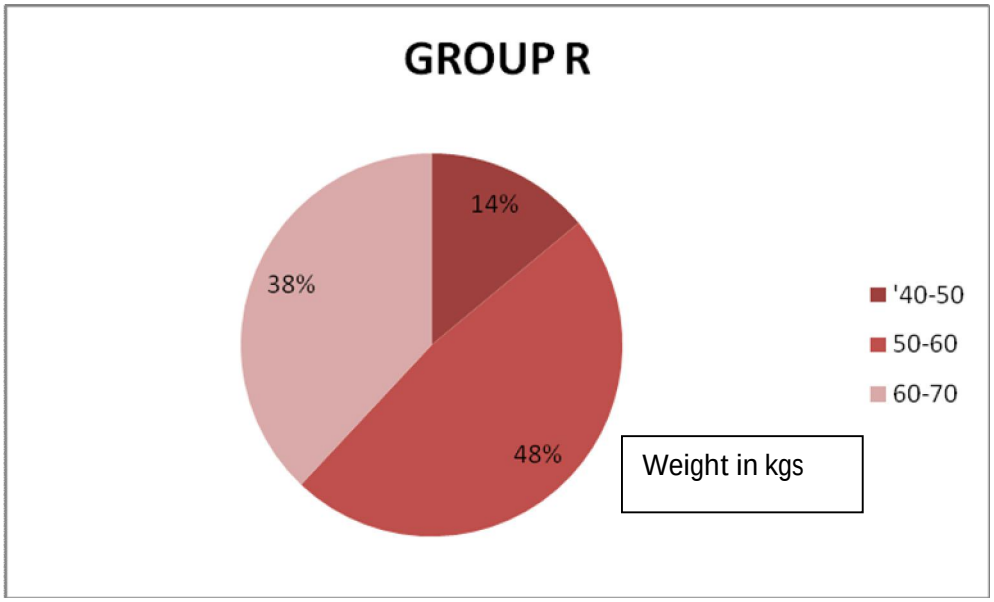

GROUP R
26%
18%
22%
34%
'20-30
30-40
40-50
50-60

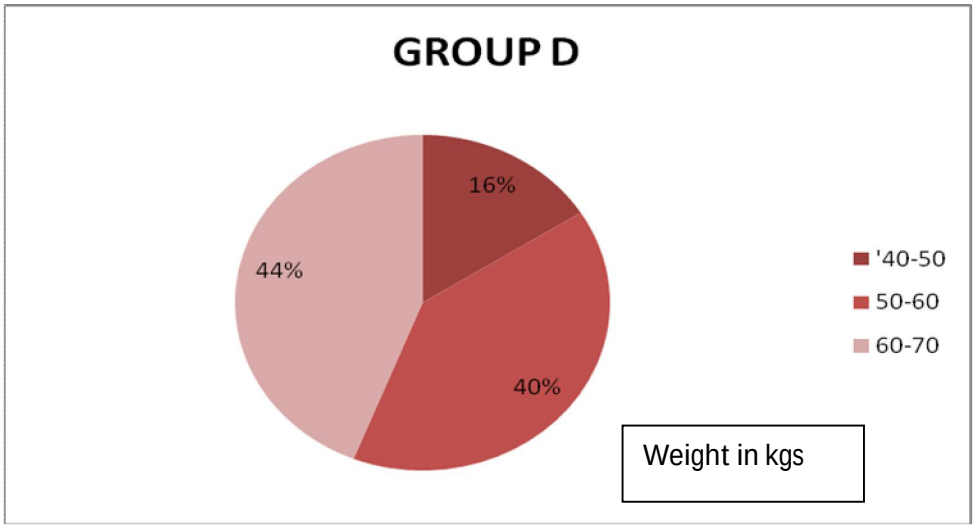

GROUP D
6%
18%
42%
34%
'20-30
30-40
40-50
50-60

WEIGHT (student's t test)

	No. of cases	**Mean ± S.D**	**p value**
Group R	50	58.8±6.2	0.4840
Group D	50	57.9± 6.6	

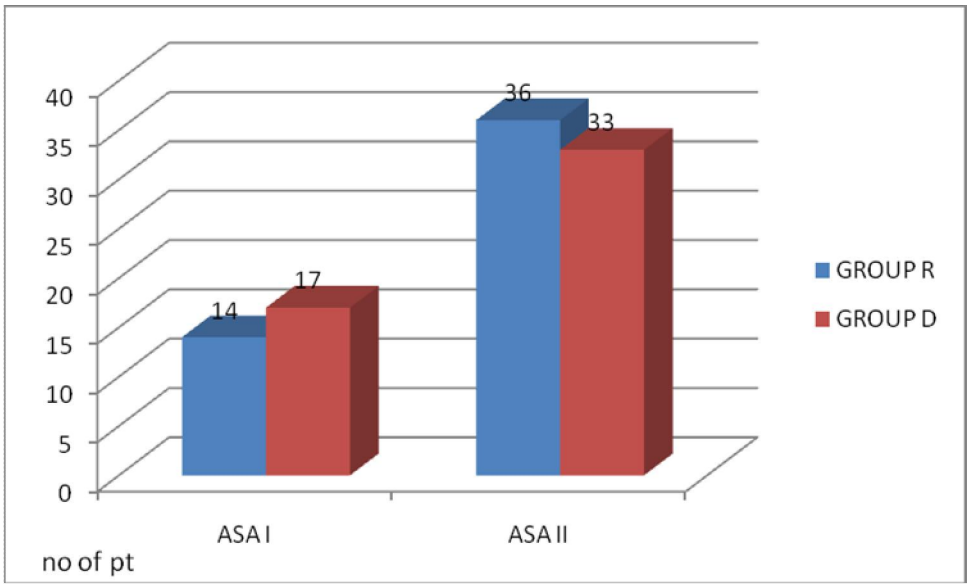
The mean weight in kgs was 58.8± 6.2 in Group R and 57.9± 6.6 in Group D. Both the groups did not differ significantly (P>0.05).


GROUP R
14%
38%
48%
'40-50
50-60
60-70
Weight in kgs


GROUP D
16%
44%
40%
'40-50
50-60
60-70
Weight in kgs

ASA-PHYSICAL STATUS (Chi-square test)

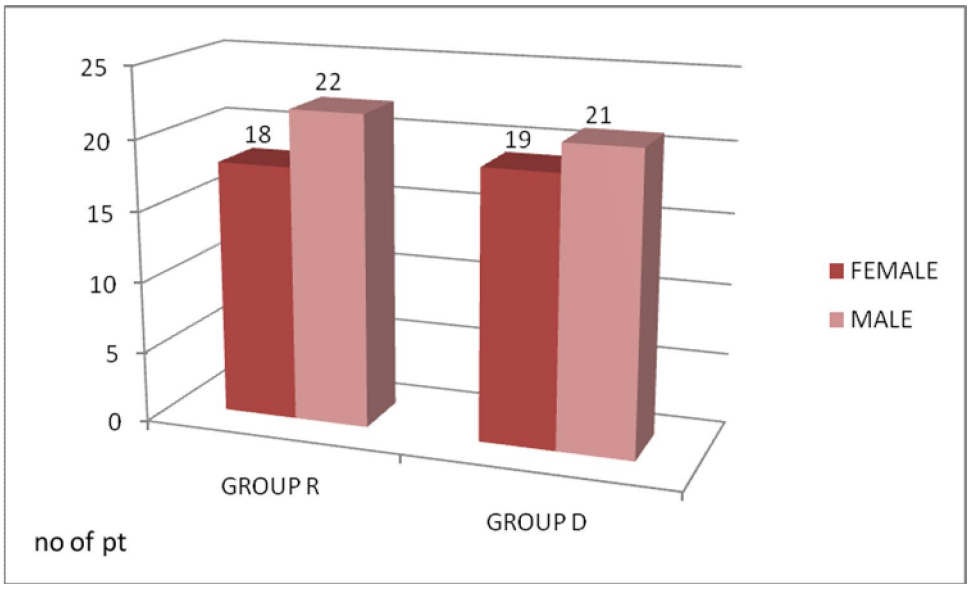
	ASA-PS I	ASA- PS II	p value
Group R	14(28%)	36(72%)	0.6654
Group D	17(34%)	33(66%)	



The percentage of ASAI patient and ASAII patients in Group R were 28% and 72% respectively while in Group D it is 34% and 66% respectively. There was no significant difference among both the groups (P>0.05).

SEX (Chi-square test)

	Female	Male	P value
Group R	18(45%)	22(55%)	0.8226
Group D	19(43%)	21(57%)	

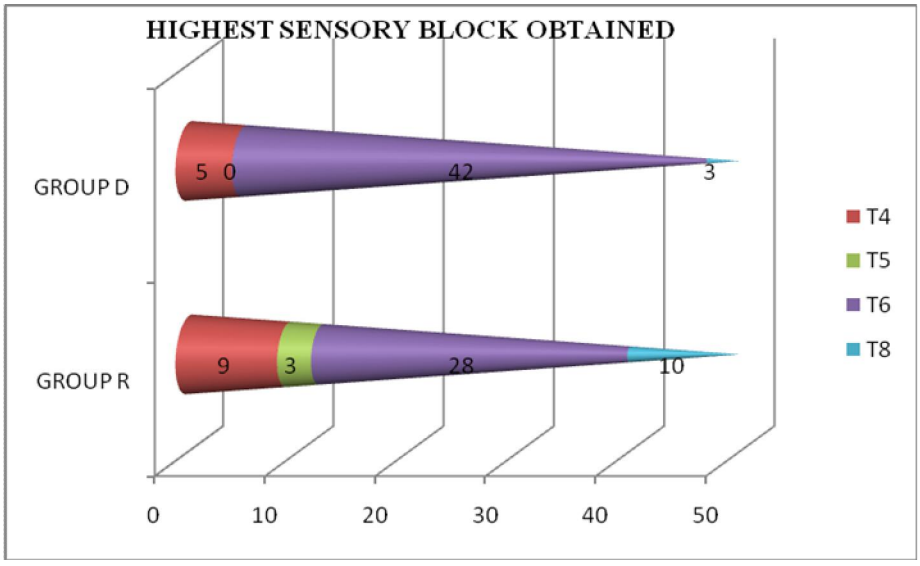


The percentage of female patients and male patients in Group R were 45% and 55% respectively while in Group D it were 43% and 57% respectively. They did not differ significantly (P>0.05).

HIGHEST SENSORY BLOCK OBTAINED(student's t test)

Level	Group R	Group D	P value
T4	9(18%)	5(10%)	0.8143
T5	3(6%)	0(0%)	
T6	28(56%)	42(84%)	
/T8	10(20%)	3(6%)	

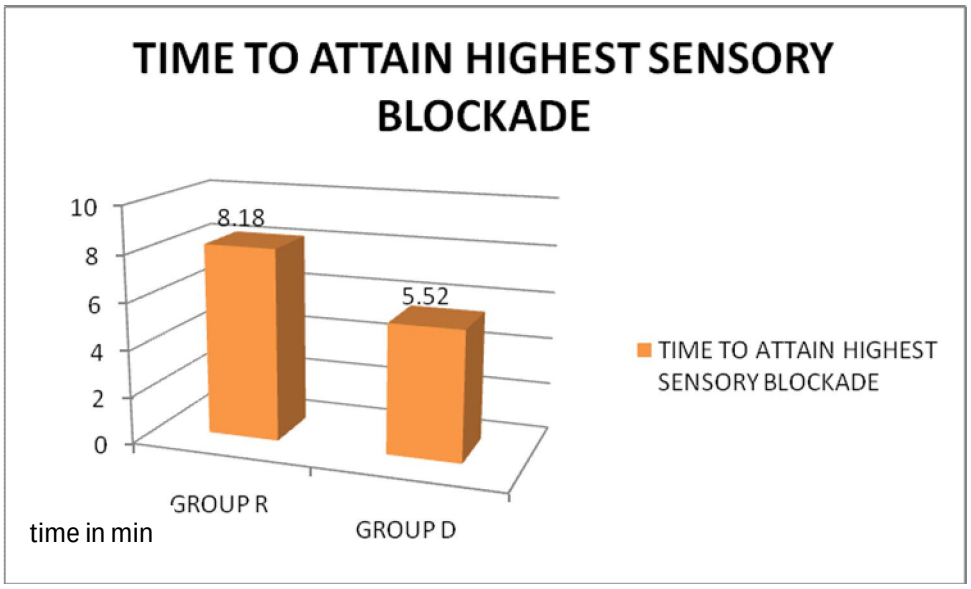
There was no difference in highest sensory level obtained in between two groups. Both group R and group D were comparable in respect to highest level of sensory block obtained (p value0.8143 i.e >0.05).



TIME TO ATTAIN HIGHEST SENSORY BLOCK (student's t test)

	No. of Cases	Mean±S.D	p value
Group R	50	8.18± 1.7921	0.0001
Group D	50	5.52±2.159	

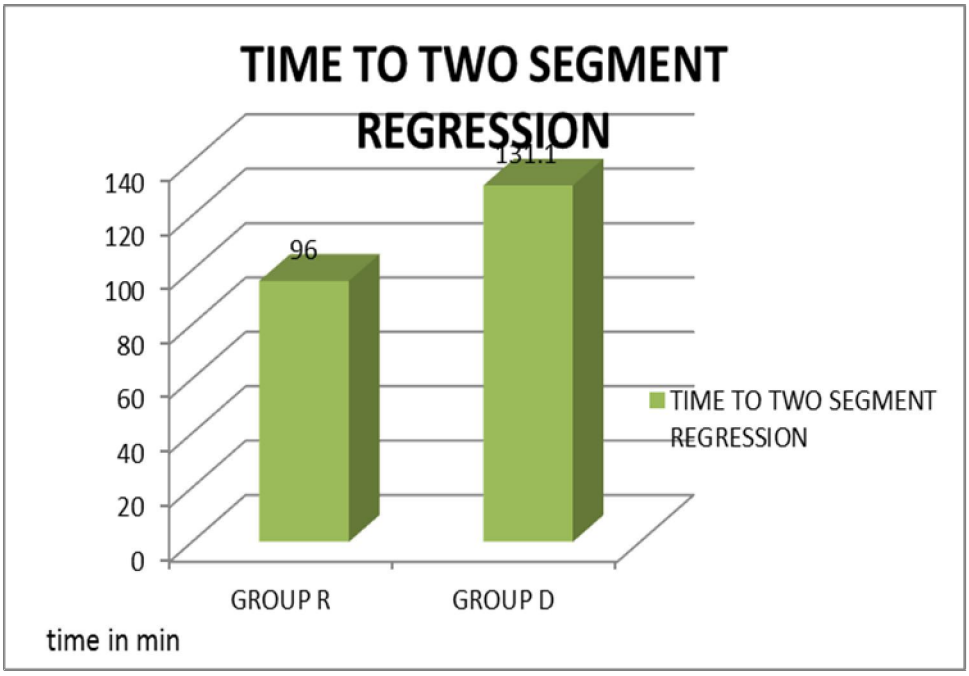
The mean time to attain highest sensory block was 8.18± 1.7921minutes in Group R and 5.52±2.159 minutes in Group D. There was significant difference among two groups in the time to attain highest sensory block (P<0.05).



TIME TO TWO SEGMENT REGRESSION (student's t test)

	No. of Cases	Mean±S.D	p value
Group R	50	96± 4.94	0.0001
Group D	50	134±6.06	

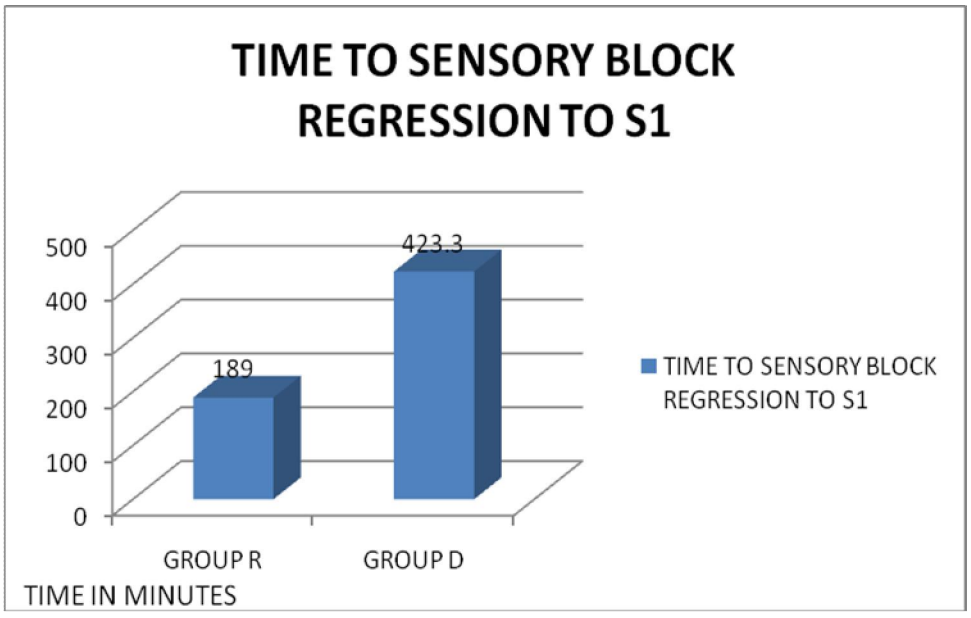
The mean time for two segment regression was 96 ± 4.94minutes in Group R and 134 ± 6.06minutes in Group D. There was significant difference among two groups in the duration two segment regression (P<0.05).



DURATION OF REGRESSION TO S1 (student's *t* test)

	No. of Cases	Mean±S.D	p value
Group R	50	189.1± 23.44	0.0001
Group D	50	423.3± 32.66	

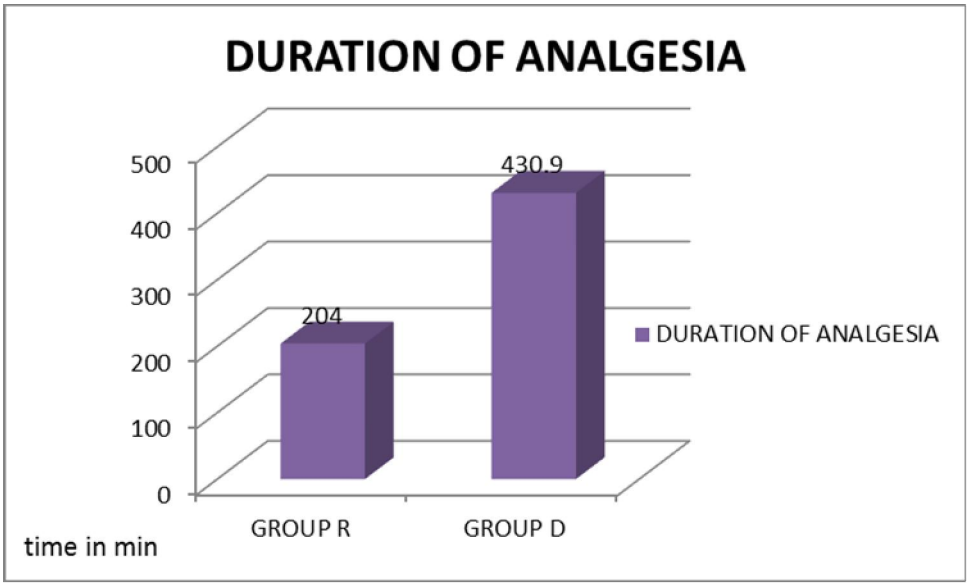
The mean duration of analgesia was 189.1± 23.44minutes in Group R and 423.3± 32.66 minutes in Group D. There was statistically significant difference among two groups in the duration of regression to S1 (P<0.05).



DURATION OF ANALGESIA (student's *t* test)

	No. of Cases	Mean±S.D	p value
Group R	50	204.7± 20.61	0.0001
Group D	50	430.9± 33.08	

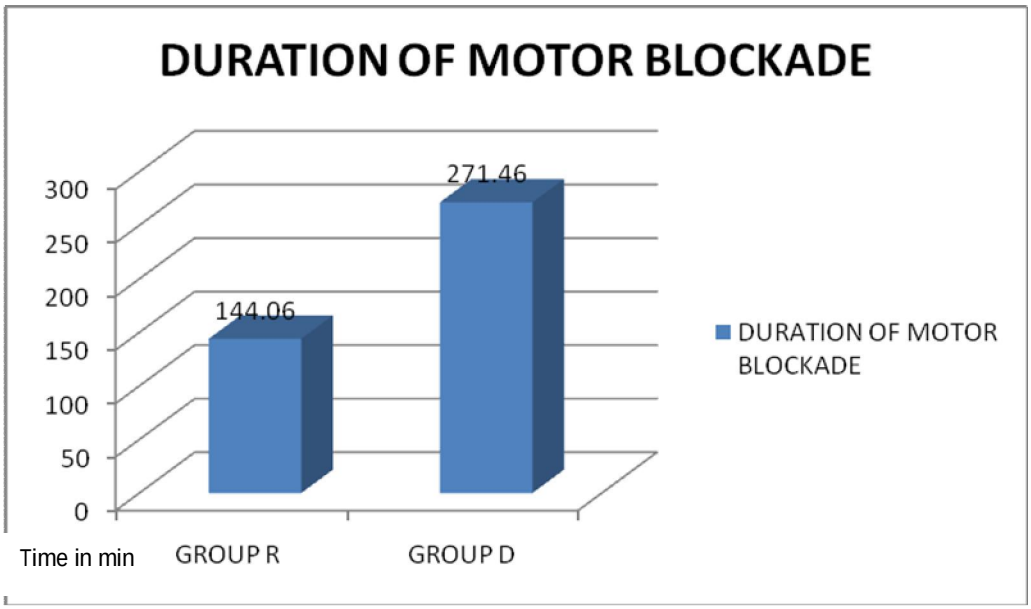
The mean duration of analgesia was 204.7 ± 20.61minutes in Group R and 430.9± 33.08minutes in Group D. There was statistically significant difference among two groups in the mean duration of analgesia (P<0.05).



DURATION OF MOTOR BLOCKADE (student's *t* test)

	No. of Cases	Mean±S.D	p value
Group R	50	144.06 ± 18.75	0.0001
Group D	50	271.46 ± 33.40	

The mean duration of motor blockade was144.06 ± 18.75 minutes in Group R and 271.46 ± 33.40 minutes in Group D. There was statistically significant difference among two groups in the mean duration of motor blockade (P<0.05).

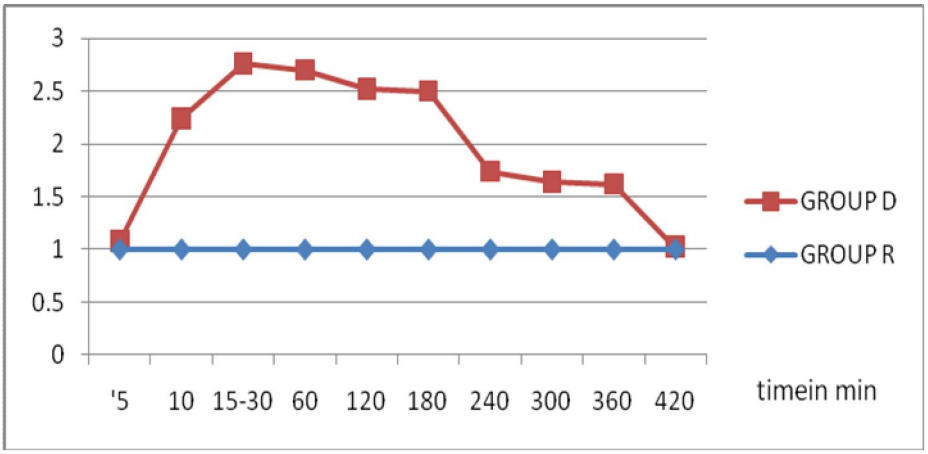


FOUR POINT VERBAL RATING SCALE (student's t test)

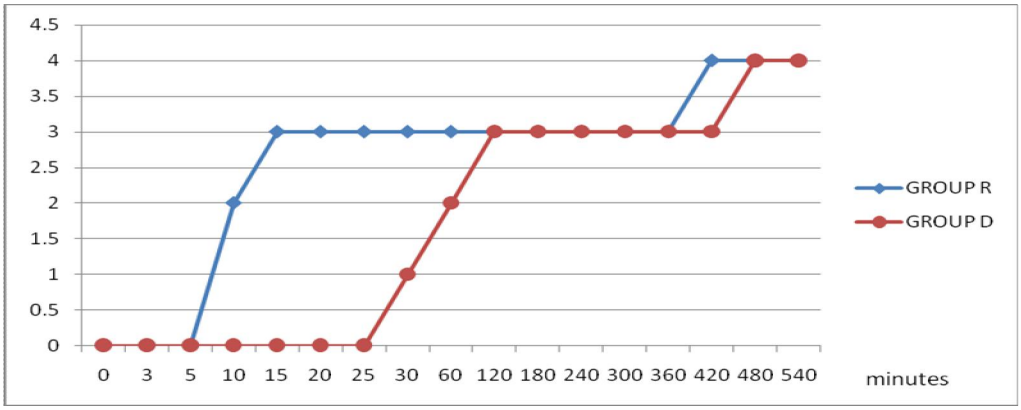
Time in Minutes	No. of Cases	Group R	Group D	P Value
5	50	1	1.08±0.2740	0.0416
10	50	1	2.24±0.4314	0.0001
15-30	50	1	2.765±0.425	0.0001
60	50	1	2.7±0.4529	0.0001
120	50	1	2.52 ±0.504	0.0001
180	50	1	2.5±0.505	0.0001
240	50	1	1.74±0.4646	0.0001
300	50	1	1.64±0.4848	0.0001
360	50	1	1.62±0.4848	0.0001
420	50	1	1.02±0.1414	0.3197

Sedation as assessed by four point verbal scale was significant during 10min-360min of the observing period between the two groups while not significant during first 5mins and after 360min as shown by the p values.

FOUR POINT VERBAL RATING SCALE



VISUAL ANALOGUE SCORE

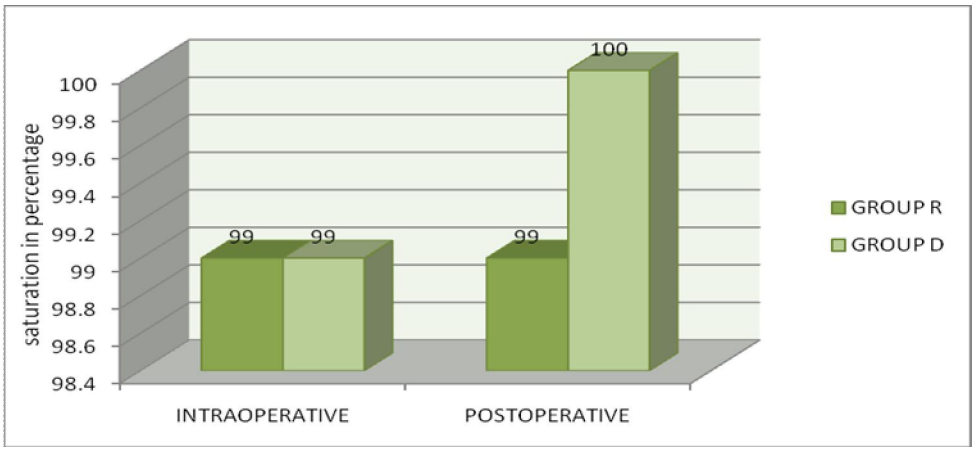


VISUAL ANALOGUE SCORE (student's t test)

Time in Minutes	No. of Cases	Group R	Group D	P value
30	50	1.79±1.506	0.125±0.35	0.0001
60	50	3.14±0.78	1.78±0.79	0.0001
120	50	3.18±0.74	2.74±0.44	0.0005
180	50	3.18±0.74	2.74±0.44	0.0003
240	50	3.18±0.74	2.52±0.5	0.0001
300	50	3.18±0.74	2.52±0.5	0.0001
360	50	3.18±0.74	2.72±0.45	0.0003
420	50	4±0	2.42±0.57	0.0001
480	50	4±0	2.88±0.65	0.0001
540	50	4±0	2.92±0.92	0.0001

VAS score between group R and group D were found to be significant during the whole period of observation ($p<0.05$).

SATURATION (Chi-square test)



Intraoperative	No. of Cases	Mean ± S.D	P value
Group R	50	99±0.0047	0.9601
Group D	50	99± 0.0027	
Postoperative	**No. of Cases**	**Mean ± S.D**	
Group R	50	100±0.00106	
Group D	50	99± 0.001118	

There was no statistical significant between two groups in saturation both during intraoperative and postoperative observation period (p value >0.05).

INTRAOPERATIVE PULSE RATE (student's *t* test)

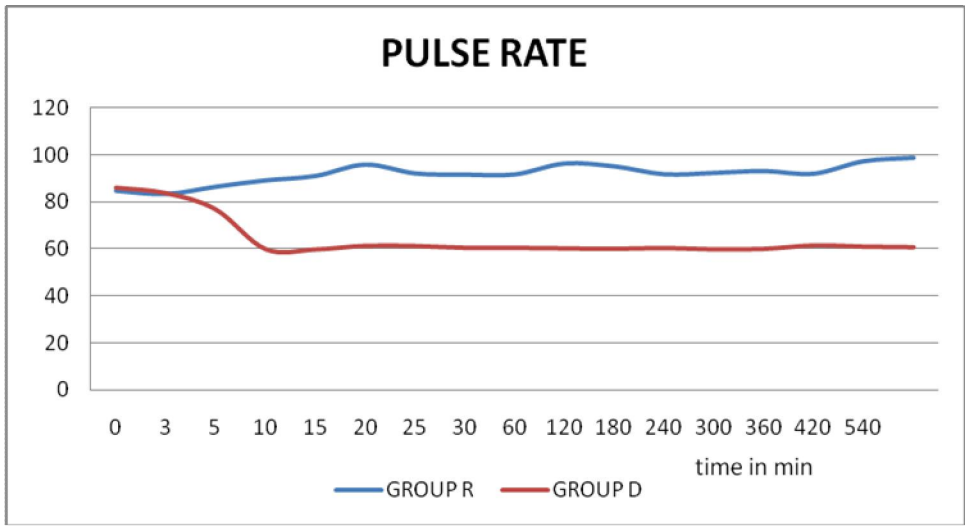
	No. of Cases	Mean ± S.D	p value
Group R	50	90.1± 4.39	0.0001
Group D	50	67.136 ±10.7	

The mean heart rate in Group R was 90.1± 4.39 and in Group D was 67.136 ±10.7, which was found to be statistically significant ($p<0.05$).

POSTOPERATIVE PULSE RATE (student's *t* test)

	No. of Cases	Mean ± S.D	p value
Group R	50	94.25± 2.818	0.0001
Group D	50	60.64 ±0.599	

The mean heart rate in Group R 94.25± 2.818was and in Group D was 60.64 ±0.599, which was found to be statistically significant ($p<0.05$).


PULSE RATE
120
100
80
60
40
20
0
0 3 5 10 15 20 25 30 60 120 180 240 300 360 420 540
time in min
GROUP R
GROUP D

MEAN ARTERIAL PRESSURE

INTRAOPERATIVE PERIOD (student's *t* test)

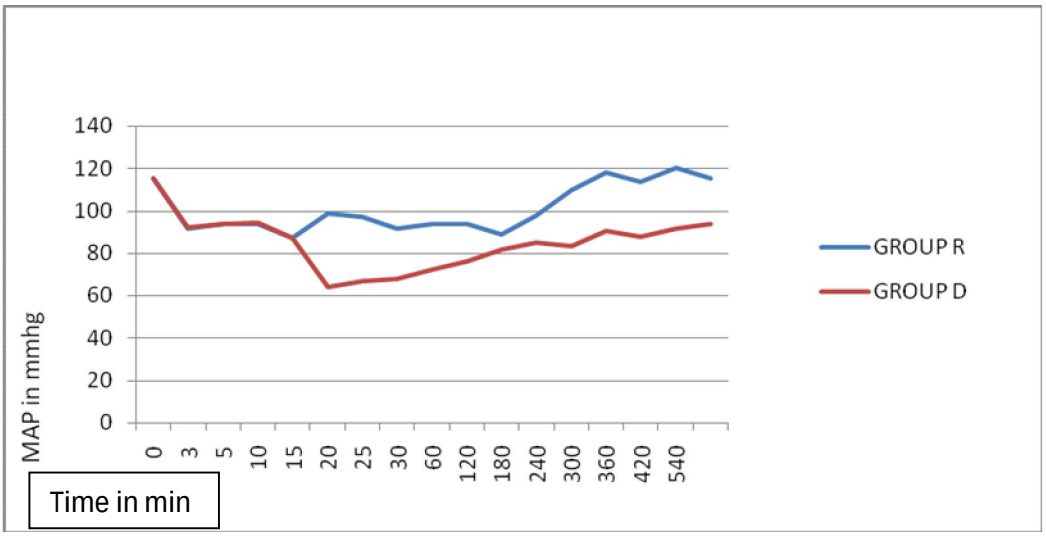
	No. of Cases	Mean ± S.D	p value
Group R	50	95.76± 7.45	0.0001
Group D	50	83.04±16.12	

The intraoperative mean arterial pressure in Group R was 95.76± 7.45 and in Group D was 83.04±16.12 which was statistically found to be significant ($p<0.05$).

POSTOPERATIVE PERIOD (student's *t* test)

	No. of Cases	Mean ± S.D	p value
Group R	50	109 ± 11.53	0.0001
Group D	50	87.74 ± 4.46	

The postoperative mean arterial pressure in Group R was109± 11.53and in Group D was87.74±4.46which was statistically found to be significant ($p<0.05$)


140
120
100
80
60
40
20
0
MAP in mmhg
0
3
5
10
15
20
25
30
60
120
180
240
300
360
420
540
Time in min
GROUP R
GROUP D

SIDE EFFECTS (Chi-square Test)

Time in Minutes	No. of Cases	Group R	Group D	p value
Hypotension	50	6	9	0.5766
Bradycardia	50	3	7	0.3178
Nausea	50	7	3	0.3178
Vomiting	50	7	3	0.3178
Shivering	50	19	2	0.0002
Dry mouth	50	3	3	1.0000

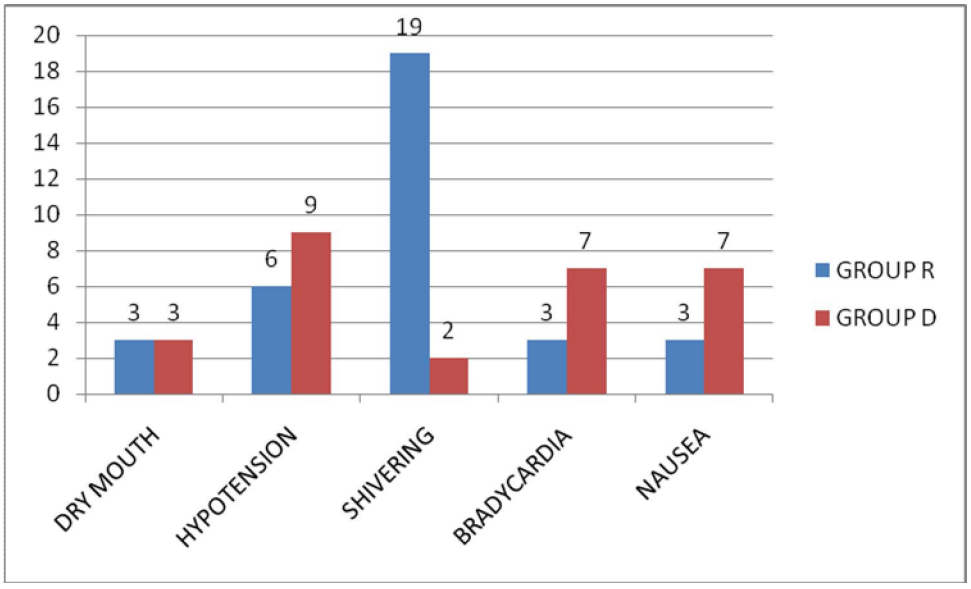
The incidence of hypotension in Group R was 12% and in Group D was 18% which was statistically not significant ($p>0.05$).

The incidence of bradycardia in Group R was 6% and in Group D was 14% and there was statistically no significant difference in both groups ($p>0.05$).

The incidence of nausea and vomiting in Group R 14% and in Group D was 6% which was statistically not significant ($p>0.05$)

The incidence of shivering in Group R was 38% and in Group D was 4% and there was statistically significant difference in both groups ($p<0.05$).

The incidence of dry mouth in Group C was 6% and in Group D was 6%. Statistically there was no significant difference in both groups (p>0.05).



DISCUSSION

An ideal adjuvant should provide a longer duration of analgesia and better hemodynamic stability. There is a reduced requirement of analgesia with the use of intrathecal adjuvants due to the property of augmentation of local anaesthetic effects, thereby prolonging the duration of analgesia. To avoid neuraxial opioid induced adverse effects such as respiratory depression, nausea, vomiting, urinary retention and pruritus[25 - 27] , α-2 agonists are being used as an alternative intrathecal adjuvants. Introduction of this newer agent dexmedetomidine has increased the wider scope of α-2 agonists usage in neuraxial blockade. Rapid onsets of local anaesthetics action, longer period of analgesia and better cardiovascular parameters have increased the wider scope of usage of dexmedetomidine in intrathecal use.

In our study 5µg of dexmedetomidine (made upto 0.5ml with normal saline) was added to 3ml of 0.75% Ropivacaine or 3ml of 0.75% Ropivacaine with normal saline 0.5ml added. The efficacy of dexmedetomidine as an adjuvant in neuraxial analgesia was studied in 50 patients in each group who underwent elective lower limb orthopedic surgeries.

The patients in both the groups with respect to age, weight, ASA Physical status did not show statistically significant difference.

Duration of analgesia

The study had shown that addition of 5µg of dexmedetomidine to 3ml of 0.75% Ropivacaine in group D prolongs the duration of analgesia about 2 times of the plain Ropivacaine group R. In group R duration of analgesia was only 204.7 ± 20.61mins compared to group D which was almost 2 times of group R 430.9 ± 33.08 mins. This result was concurrent with the Gupta R et al (2011; 55:347-51) study where they concluded that the duration of analgesia was prolonged for about 478±20.9 minutes in group D compared to group R which as only 241.67±21.67 minutes duration. This result was also correlated with the study **Shukla et al** where they concluded that onset of anesthesia was faster with prolonged duration of analgesia in the group (D) and also in the studies conducted by Kallio et al[11] (2011) & Vieira et al[3] (2004).

TIME TO REGRESSION OF BLOCK TO S1

The time to regression of sensory blockade to S1 in group D was 423.3 ± 32.66 mins and in Group R was 189±23.44 mins which is nearly three times for dexmedetomidine group when compared to plain ropivacaine in our study and it is statistically significant.This result was correlated with following studies done by different authors.

1. **Gupta R et al (2011):** had found out that the mean time for S2 segment regression was 468.3 ± 36.78 minutes in group D and 239.33 ± 16.8 minutes in group R.

2. **Kanazi GE et** al: had observed that patients in dexmedetomidine group D and Clonidine group C had early onset time of motor block and a prolonged sensory and motor regression times than plain bupivacaine group B which was statistically significant. The mean time of S1 segment regression was 303 ±75 mins in group D, 272±38 mins in group C and 190±48 mins in group B.

3. **Gupta R et al (2011):** had observed that the mean time of sensory level regression to S1 dermatome was 476 ± 23 mins in dexmedetomidine group D and 187 ± 12 mins in fentanyl group F (*P*<0.001).

4. **Shukla et al**: had found that faster onset and longer duration of anesthesia in the dexmedetomidine group (D).

Duration of motor blockade

There is a significant prologation in duration of motor blockade in group D with 271.46±33.40 mins when compared to group R i.e. 144.06±18.75 mins. These results correlate with following studies.

1. **Kanazi et al**: had observed that the motor block duration was 250 +/-76 mins in dexmedetomidine group D, 216±35 mins in clonidine group C and 163 ± 47 mins in plain bupivacaine group B.

2. **Gupta et al**: evaluated the motor block duration was about 421 ± 21 min in dexmedetomidine group D and about 149±18 min in fentanyl group F (*P*<0.001). They found out that the spinal

dexmedetomidine is associated with longer duration of motor and sensory block.

3. **Al-Mustafa MM et al** concluded that Dexmedetomidine has a effect on the onset and regression of sensory and motor block in a dose dependent manner, when used as an intrathecal adjuvant to bupivacaine.

4 **Eid HEA et al** [22] concluded that the Intrathecal dexmedetomidine in two different doses (10μg and 15μg) significantly prolong the anesthetic and analgesic effects of intrathecal bupivacaine in a dose-dependent manner.

5 **Shukla et al** [16] recorded onset time to reach peak sensory and motor level, the regression time for sensory and motor block, hemodynamic changes and side effects .They found that faster onset of anesthesia with prolonged duration of analgesia in the dexmedetomidine group.

Sedation score

The results of our study clearly indicate the sedation score between the two groups was similar in the initial period after study drug administration and they had profound sedation but arousable by gentle tactile stimulation (i.e. four point verbal rating scale of 2). After 10mins, the percentage of dexmedetomidine group patients who have scored

higher sedation scores is more compared to group R. there was a significant sedative effects for dexmedetomidine group of patients.

Hemodynamic stability

The heart rate, mean arterial pressure remained stable both during introperative and postoperative period. Although a fall in heart rate and blood pressure (both systolic and diastolic) was noted in both the groups, it never decreased below the 20% of baseline values. But hypotension and bradycardia were observed more in group D patients which is statistically significant and it is correlated with the results of Gupta et al 2011, kanazi et al.

SIDE EFFECTS

The incidence of bradycardia in Group R was 30% and in Group D was 70% and there was statistically no significant difference in both groups ($p>0.05$). The incidence of nausea and vomiting in Group R was 70% and in Group D was 30% which was statistically not significant ($p>0.05$). The incidence of shivering in Group R was 90% and in Group D was 10% and there was statistically significant difference in both groups ($p<0.05$).

The incidence of dry mouth in Group C was 50% and in Group D was 50%. Statistically there was no significant difference in both groups ($p>0.05$).These results had concurrence with the results of **Eid HEA et al**

VAS SCORE

VAS score between group R and group D were found to be significant during the whole period of observation ($p<0.05$) which correlated with study done by **Gupta et al** which showed the maximum visual analogue scale score for pain was less in group D (4.4±1.4) as compared to group R (6.8±2.2).

SUMMARY

This double blinded prospective randomized controlled study was done to evaluate the duration of analgesia, sensory and motor blockade, sedation and adverse effects of dexmedetomidine 5µg with 0.75% isobaric Ropivacaine vs. plain 0.75% isobaric Ropivacaine given intrathecally in patients who underwent lower limb orthopedic surgeries.

The following observations were made:

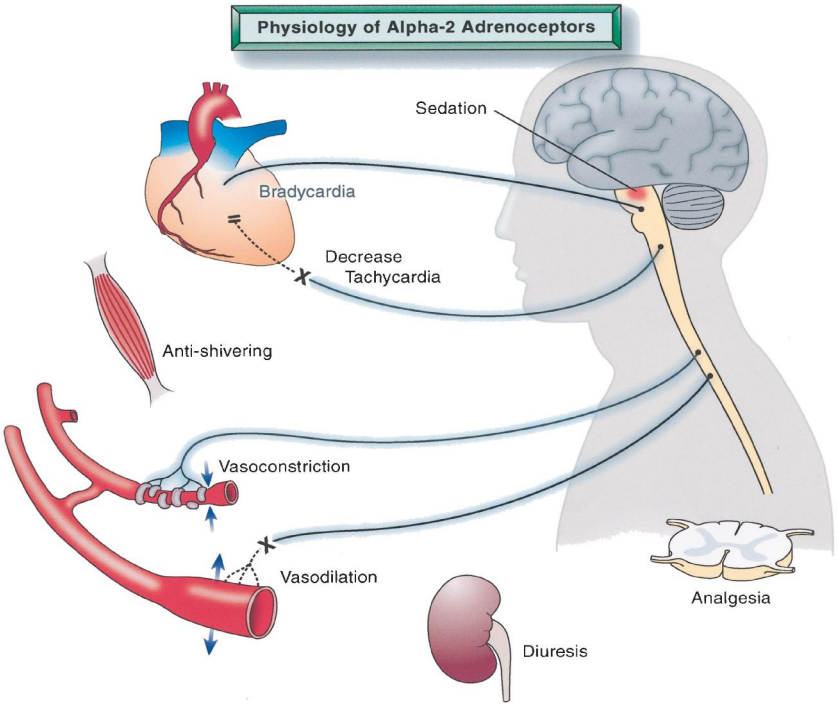
1. The addition of 5ug Dexmedetomidine to 0.75% Ropivacaine significantly prolonged the duration of analgesia.
2. The addition of dexmedetomidine significantly prolonged the time for demand analgesia.
3. The addition of dexmedetomidine intrathecally produced sedation that was arousable for many hours compared to plain ropivacaine group
4. The incidence of side effects such as hypotension and bradycardia were more in patients who received dexmedetomidine but were able to manage easily with inj.ephedrine and inj.atropine. But shivering was greatly reduced in dexmedetomidine.
5. No episode of respiratory depression was noted in both the study groups which are more common with opioids.

CONCLUSION

To conclude 5ug of dexmedetomidine seems to be a better adjuvant to intrathecal isobaric Ropivacaine (0.75%) in increasing the duration of analgesia, prolonging the duration of sensory and motor blockade with minimal side effects.


Rx
ROPIVACAINE
HYDROCHLOR
INJECTION US
ROPIN
Local Anaesthetic
Preservative not
रोपिन 0.75%
4mL


Rx
Dexmedetomidine
Hydrochloride Inj
DEXTOMID
For I.V. Infusion after
Each ml contains:
Dexmedetomidine
Hydrochloride equivalent
Dexmedetomidine
Water for Injections I.P.
MADE IN INDIA BY:
NEON LABORATORIES
Boisar Road, Palghar (Thane)



Physiology of α2 adrenergic receptors

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INFORMATION TO PARTICIPANTS

Investigator :

Name of the Participant :

Title

Comparison of the Duration of Analgesia, Duration of Sensory And Motor Blockade and Incidence of Side Effects of Intrathecal 0.75% Isobaric Ropivacaine with Combination of 0.75% Isobaric Ropivacaine And Dexmedetomidine.

You are invited to take part in this research study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

You are being asked to participate in this study being conducted in The Department of Anaesthesiology, Chengalpattu medical college hospital, Chengalpattu.

What is the Purpose of the Research

For orthopaedic lower limb surgeries, intrathecal anesthesia is administered with the drug 0.75% Ropivacaine with or without adjuvants. This gives the pain relief for a reasonable period of time. In this we study by adding Dexmedetomidine (selective alpha 2 agonists) to intrathecal 0.75% Ropivacaine and its effects on post operative analgesia.

The Study Design

All the patients in the study will be divided into two equal groups. One group will receive intrathecal 0.75% Ropivacaine and another group will receive intrathecal 0.75% Ropivacaine plus Dexmedetoimidine 5µg

Benefits

By review of previous study post operative analgesia after intrathecal 0.75% Ropivacaine with Dexmedetomidine will be prolonged. This drug also has sedative property which reduces the conception of other sedative drugs.

Discomforts and risks

Hypotension and Bradycardia- common side effects of sedative $\alpha 2$ agonists. Rarely nausea and vomiting also occur. Inj.Ondensetron will be given for vomiting. Hypotension and Bradycardia will be treated with Inj.Ephedrine, Inj.Atropine respectively.

And if you do not want to participate you will have alternative of setting the standard treatment and your safety is our prime concern.

Time :

Date :

Place : Signature/Thumb impression of the Patient

Patient Name :

Signature of the Investigator : _____

Name of the Investigator : _____

PROFORMA

Comparison of the Duration of Analgesia, Duration of Sensory And Motor Blockade and Incidence of Side Effects of Intrathecal 0.75% Isobaric Ropivacaine with Combination of 0.75% Isobaric Ropivacaine And Dexmedetomidine.

Name Age/Sex IP No Weight____kgs Height ____ cms

Diagnosis Procedure

H/O Previous surgery:

Co morbid illness:

Personal history:

H/O Allergy:

General examination:

Built & Nourishment

Pallor / Cyanosis / Clubbing / Icterus / Pedal edema

PR /min NIBP mm/Hg RR / min

Airway examination: MPC Neck movements

Systemic examination: CVS RS P/A CNS

INVESTIGATIONS

Hb%: Platelet count: BT: CT:

Blood sugar: Blood urea: Serum creatinine:

ECG: Chest X ray: ECHO:

OPINION:

Assessment no & Date ASA Physical status I/II

Pre operative preparation:

NPO: Premedication:

PROCEDURE:

Preloading: Pre op: PR / min, BP mm/Hg, SpO2 %

Position: Study group: Spinal needle:

Time	**Events**	**PR/ min**	**NIBPmm/ Hg**	**SpO_2 %**	**Sensory level**	**Motor blockade**	**VAS**	**Two segment regression**	**IV Fluids**	**Side effects**
0 min										
3 min										
5 min										
10 min										
15 min										
20 min										
25 min										
30 min										

Time	Events	PR/ min	NIBPmm/ Hg	SpO_2 %	Sensory level	Motor blockade	VAS	Two segment regression	IV Fluids	Side effects
I hr										
2 hrs										
3hrs										
5 hrs										
6hrs										
7hrs										
8hrs										
9hrs										

Rescue Analgesia:

Duration of sensory blockade

Duration of motor block

MASTER CHART
INTRATHECAL ISOBARIC 0.75%ROPIVACAINE

S. No	Name	Age	Sex	Wt	Procedure	ASA-PS	Highest sensory level obtained	Time to attain highest sensory level	Duration of two point regression	Regression of motor blockade to bromage 0	Duration of regression to s1 segment	Duration of analgesia (in minutes)
1	Palani	48	M	60	# Both bone leg iln	II	T4	8	90	125	210	220
2	Saravanan	48	M	58	# Patella right tension band wiring	II	T6	10	100	136	210	215
3	Arumugam	52	M	50	# Femur neck orif	I	T6	7	90	135	200	210
4	Kumaresan	36	M	55	# Femur neck orif	I	T6	7	100	125	160	180
5	Sivaraj	60	M	67	# Patella right tension band wiring	II	T6	8	100	146	210	225
6	Indhu	45	F	65	#patella right tension band wiring	I	T8	8	90	155	205	225
7	Kalpana	31	F	48	#both bone leg iln	I	T4	11	100	145	200	220
8	Kanchana Devi	35	F	46	Raw area leg ssg	I	T8	13	90	156	220	220
9	Vijay	58	M	55	# Both bone leg iln	II	T6	9	100	125	160	180
10	Krishnaveni	27	F	55	# Patella right tension band wiring	I	T8	6	100	165	220	225
11	Kumar	60	m	67	# Femur neck orif	ii	t6	7	90	140	160	180
12	Kareema begum	29	f	54	# Both bone leg iln	i	t8	8	100	155	220	225
13	Madan	36	m	59	# Patella right tension band wiring	i	t4	9	90	115	160	180
14	Hariharan	53	m	56	#Both bone legiln	i	t6	11	100	115	160	180
15	Anandan	45	m	64	# Femur neck orif	i	t6	5	100	165	220	225
16	Perumalpitchay	58	m	59	# Patella right tension band wiring	ii	t8	8	90	115	160	180

17	Pugazhenthi	44	f	57	#Both bone leg iln	i	t6	7	100	165	210	225
18	Nagaraj	46	m	63	#Patella left tension band wiring	i	t4	7	90	115	160	180
19	Dillibabu	43	m	68	#Both bone leg iln	i	t6	8	100	175	220	225
20	Shehim begum	37	f	56	#Both bone leg iln	i	t6	10	100	125	160	180
21	Akkaiah	40	m	67	#Patella right tension band wiring	i	t6	12	90	155	205	225
22	Ramachandran	59	m	62	Raw area leg ssg	ii	t6	9	100	105	160	180
23	Velmurugan	34	m	58	# Femur neck orif	i	t4	7	90	155	220	225
24	Sivagami	21	f	45	# Both bone leg iln	ii	t6	6	100	105	160	180
25	Vasantha	22	f	50	Raw area leg ssg	i	t4	7	100	115	160	180
26	Dhanush	28	m	60	# Both bone leg iln	i	t6	7	90	155	200	225
27	Mumtaj	37	f	55	#Both bone leg iln	i	t6	5	100	165	160	180
28	Rakkaiyee	40	f	67	#Patella right tension band wiring	i	t6	6	90	145	180	225
29	Ram	59	m	62	Raw area leg ssg	ii	t8	9	100	135	160	180
30	Mukunth	34	m	58	#Femur neck orif	i	t6	8	100	125	160	180
31	Krishna	37	m	55	#Patella right tension band wiring	i	t8	9	90	155	180	225
32	Kumari	60	f	67	#Femur neck orif	i	t6	11	100	145	170	180
33	Katheeja	29	f	64	#Both bone leg iln	i	t6	5	90	165	215	225
34	Madhu	36	m	59	#Patella right tension band wiring	i	t6	6	100	135	170	185
35	Hari	53	m	56	#Both bone leg iln	i	t5	8	100	135	165	180

36	Anandan	48	m	64	#Femur neck orif	ii	t6	8	90	175	200	225
37	Pitchay	58	m	59	#Patella right tension band wiring	ii	t6	8	100	135	180	180
38	Pushparani	44	f	57	#Both bone leg iln	i	t6	8	90	155	215	225
39	Raja	46	m	63	#Patella left tension band wiring	i	t5	9	100	135	175	180
40	Babu Raj	43	m	68	#Both bone leg iln	i	t8	9	100	156	210	220
41	Begum	37	f	56	#Both bone leg iln	i	t6	11	90	165	210	215
42	Muthamma	40	f	67	#Patella right tension band wiring	i	t4	9	100	144	200	210
43	Raman	59	m	62	Raw area leg ssg	ii	t8	9	90	135	170	180
44	Velu	34	m	58	#Femur neck orif	i	t6	8	100	155	210	225
45	Sivam	21	m	45	#Both bone leg iln	ii	t4	8	100	165	205	225
46	Vasu	22	f	50	Raw area leg ssg	i	t6	8	90	165	210	220
47	Akash	28	m	60	#Both bone leg iln	i	t8	8	100	165	220	220
48	Mangai	37	f	55	#Both bone leg iln	i	t6	7	90	160	190	210
49	Rakky	40	f	67	#Patella right tension band wiring	i	t4	6	100	145	180	215
50	ranjith reddy	59	m	62	raw area leg ssg	ii	t5	11	100	155	190	210

ORIF-OPEN REDUCTION AND INTERNAL FIXATION
SSG-SPLIT SKIN GRAFT
ILN-INTERLOCKING NAIL

INTRATHECAL ISOBARIC 0.75%ROPIVACAINE PLUS DEXMEDETOMIDINE

S. No	Name	Age	Sex	Weight	Procedure	ASA-PS	Highest sensory level obtained	Time to attain highest sensory level	Duration of two point regression	Regression of motor blockade to bromage 0	Duration of regression to s1segment	Duration of Analgesia (in minutes)
1	Gopal	55	m	55	#patella right tension band wiring	ii	t6	3	140	275	425	435
2	Samy	40	m	65	raw area leg ssg	i	t8	4	135	236	485	490
3	Subramaniam	35	m	59	#femur neck orif	i	t6	3	130	235	420	430
4	Seneka	35	f	53	#both bone leg iln	i	t6	5	140	225	380	390
5	Selvam	46	m	66	raw area leg ssg	i	t6	6	120	246		380
6	Sumathi	29	f	54	#both bone leg iln	i	t6	3	140	255	370	375
7	Varadarajan	32	m	58	#patella right tension band wiring	i	t6	4	135	245	380	390
8	Saranya	40	f	52	raw area leg ssg	i	t6	4	130	256	420	490
9	Sekar	45	m	68	#femur neck2orif	ii	t6	4	140	225	480	485
10	Panchatcharam	55	m	65	#both bone leg iln	ii	t6	4	120	265	420	430
11	Muuniyammal	45	f	64	#patella right tension band wiring	i	t6	5	140	240	430	435
12	Vijaya	50	f	55	raw area leg ssg	ii	t6	6	135	255	485	490
13	Arumugam	48	m	62	#femur neck orif	i	t4	5	130	265	420	425
14	Kumaravel	48	m	56	#both bone leg iln	i	t6	7	140	265	420	430
15	Adhilakshmi	53	f	48	raw area leg ssg	i	t6	8	120	265	485	490

16	Andavan	60	M	61	#both bone leg iln	II	T6	5	140	215	390	395
17	Chandra	45	F	54	#patella right tension band wiring	I	T6	9	135	265	410	430
18	Devaraj	40	M	46	tv&gj	II	T6	5	130	275	465	470
19	Pushparaj	49	M	67	#patella right tension band wiring	I	T6	5	140	285	390	395
20	Saravanan	48	M	54	raw area leg ssg	I	T6	8	130	265	425	430
21	Mohammed Kadar	46	M	65	#femur neck orif	I	T6	7	140	255	440	445
22	Meenal	45	F	68	#both bone leg iln	II	T6	7	135	305	405	410
23	Ramesh	30	M	61	raw area leg ssg	I	T6	8	130	285	415	430
24	Murugan	45	M	59	#both bone leg iln	I	T6	8	140	285	390	395
25	Thangavelu	57	M	65	#femur neck orif	II	T6	8	140	225	425	430
26	Katheresan	40	M	55	#both bone leg iln	I	T6	9	140	295	440	445
27	Lakshmi	53	F	48	raw area leg ssg	I	T6	9	135	275	405	410
28	Andal	61	F	61	#both bone leg iln	II	T6	11	130	265	425	430
29	Chandra	45	F	54	#patella right tension band wiring	I	T6	3	140	235	390	395
30	Devan	41	M	47	raw area leg ssg	II	T6	3	130	295	485	490
31	Maryammal	55	F	64	#patella right tension band wirin	I	T6	4	140	255	390	395
32	Alarmelmangai	50	F	55	raw area leg ssg	II	T6	4	135	245	425	430
33	Shanmugam	48	M	62	#femur neck orif	I	T6	4	130	265	440	445
34	Sannasi	55	M	56	#both bone leg iln	I	T6	4	140	235	405	410

35	Bahagyalakshmi	53	F	48	raw area leg ssg	I	T6	5	120	335	485	490
36	Anbu	60	M	61	#both bone leg iln	II	T6	5	140	375	390	395
37	Chitra	55	F	54	#patella right tension band wiring	I	T6	6	135	335	425	430
38	David	40	M	46	tv&gj	II	T6	6	130	315	440	445
39	Pushparaj	59	M	67	#patella right tension band wiring	I	T4	5	140	335	405	410
40	Saran	58	m	54	raw area leg ssg	i	t6	5	135	256	415	420
41	Kaleem	46	m	65	#femur neck ori2	i	t6	6	130	265	465	470
42	Menaka	55	f	68	#both bone leg iln	ii	t4	3	140	244	390	395
43	Rameshwaran	30	m	61	raw area leg ssg	i	t8	5	120	265	425	430
44	Muniyaswamy	60	m	59	#both bone leg iln	i	t6	3	140	265	430	435
45	Velu	57	m	65	#femur neck orif	ii	t4	4	135	275	405	410
46	Nesamani	40	m	55	#both bone leg iln	i	t6	4	130	315	485	490
47	Lakshmiammal	60	f	48	raw area leg ssg	i	t8	3	140	305	390	395
48	Anjalakshi	51	f	61	#both bone leg iln	ii	t6	9	120	290	425	430
49	Cinthamani	55	f	54	#patella right tension band wiring	i	t4	11	140	315	440	445
50	Nanadakumar	60	m	47	raw area leg ssg	ii	t6	4	135	305	405	410

22RIF-OPEN REDUCTION AND INTERNAL FIXATION

2SG-SPLIT SKIN GRAFT ILN-INTERLOCKING NAIL

PULSE RATE –INTRATHECAL ISOBARIC 0.75%ROPIVACAINE

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
1	87	76	78	74	74	77	73	86	90	96	120	105	96	96	98	106	106
2	86	82	87	89	83	95	103	113	111	93	95	90	91	102	94	100	102
3	89	73	86	90	96	120	99	97	109	107	99	88	90	109	109	100	110
4	84	73	89	89	98	98	97	108	99	108	108	96	98	95	98	97	95
5	83	77	84	96	90	87	93	90	97	89	93	95	103	83	95	105	96
6	83	73	83	95	105	96	96	83	89	82	87	89	83	95	103	87	99
7	73	73	83	95	105	96	96	83	120	105	96	96	98	120	105	98	98
8	78	78	78	88	93	90	97	89	93	93	92	90	105	96	96	98	120
9	86	86	85	96	90	97	93	96	89	99	92	90	83	95	105	96	96
10	74	74	84	84	89	94	93	90	97	89	92	90	60	93	90	97	89
11	79	79	80	84	84	97	73	74	73	89	92	90	87	89	83	95	103
12	87	87	89	89	89	105	96	96	98	120	88	98	99	99	99	98	98
13	87	87	89	90	90	103	93	82	82	91	105	96	96	98	120	94	94
14	93	93	90	97	89	93	93	90	93	90	97	89	93	93	90	97	89
15	84	84	89	94	93	90	84	89	94	99	99	87	90	99	89	98	98
16	89	89	89	89	95	105	96	96	98	120	91	90	84	92	91	94	94
17	90	90	90	90	95	103	83	95	105	95	103	83	95	63	63	109	109
18	89	89	89	89	89	83	95	103	87	89	83	95	103	53	59	98	98
19	63	63	75	88	95	103	83	95	105	95	103	83	95	103	83	95	105
20	95	95	103	83	95	105	96	95	95	103	83	95	89	83	95	103	87

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
21	89	89	83	95	103	87	99	89	89	83	95	103	95	103	83	95	105
22	67	67	89	95	103	83	95	105	59	95	103	83	95	103	83	95	105
23	95	95	103	89	83	95	103	87	90	89	83	95	103	83	95	105	96
24	89	89	83	95	103	83	95	105	92	95	103	83	83	95	103	87	99
25	95	95	103	89	83	95	103	87	91	89	83	95	95	103	83	95	105
26	79	79	80	84	84	97	73	74	73	89	92	90	87	89	83	95	103
27	87	87	89	89	89	105	96	96	98	120	88	98	99	99	99	98	98
28	87	87	89	90	90	103	93	82	82	91	105	96	96	98	120	94	94
29	93	93	90	97	89	93	93	90	93	90	97	89	93	93	90	97	89
30	84	84	89	94	93	90	84	89	94	99	99	87	90	99	89	98	98
31	74	74	84	84	89	94	93	90	97	89	92	90	60	93	90	97	89
32	79	79	80	84	84	97	73	74	73	89	92	90	87	89	83	95	103
33	87	87	87	89	90	105	96	96	98	120	88	98	99	99	99	98	98
34	87	93	93	90	97	103	93	82	82	91	105	96	96	98	120	94	94
35	93	84	84	89	94	93	93	90	93	90	97	89	93	93	90	97	89
36	84	74	74	84	84	90	84	89	94	99	99	87	90	99	89	98	98
37	89	79	79	80	84	105	96	96	98	120	91	90	84	92	91	94	94
38	90	87	87	89	90	103	83	95	105	95	103	83	95	63	63	109	109
39	89	93	93	90	97	83	95	103	87	89	83	95	103	53	59	98	98
40	63	84	84	89	94	103	83	95	105	95	103	83	95	103	83	95	105
41	95	74	74	84	84	105	96	95	95	103	83	95	89	83	95	103	87
42	89	79	79	80	84	87	99	89	89	83	95	103	95	103	83	95	105

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
43	67	87	87	89	90	83	95	105	59	95	103	83	95	103	83	95	105
44	87	87	89	90	97	95	103	87	90	89	83	95	103	83	95	105	96
45	93	93	90	89	94	83	95	105	92	95	103	83	83	95	103	87	99
46	84	84	89	84	84	95	103	87	91	89	83	95	95	103	83	95	105
47	74	74	84	84	84	97	73	74	73	89	92	90	87	89	83	95	103
48	79	79	80	89	89	105	96	96	98	120	88	98	99	99	99	98	98
49	87	87	89	90	90	103	93	82	82	91	105	96	96	98	120	94	94
50	93	93	90	97	89	93	93	90	93	90	97	89	93	93	90	97	89

PULSE RATE –INTRATHECAL ISOBARIC 0.75%ROPIVACAINE PLUS DEXMEDETOMIDINE

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300MIN	360 MIN	420 MIN	480 MIN	540 MIN
1	88	88	56	57	58	59	59	58	58	58	56	56	57	58	59	59	58
2	91	91	60	60	61	62	62	59	59	59	61	60	60	61	62	62	59
3	88	88	67	66	65	68	65	69	65	65	64	67	66	65	68	65	69
4	78	78	57	57	55	59	57	58	58	58	56	57	57	55	59	57	58
5	86	86	63	63	62	61	66	63	64	64	64	63	63	62	61	66	63
6	88	88	58	47	49	54	55	49	55	55	58	58	47	49	54	55	49
7	83	83	65	67	67	64	64	63	66	66	66	65	67	67	64	64	63
8	88	88	56	57	58	59	59	58	58	58	56	56	57	58	59	59	58
9	91	91	60	60	61	62	62	59	59	59	61	60	60	61	62	62	59
10	88	88	56	57	58	59	59	58	58	65	64	67	66	65	68	65	69
11	78	78	60	60	61	62	62	59	59	58	56	57	57	55	59	57	58
12	86	86	67	66	65	68	65	69	65	58	56	56	57	58	59	59	58
13	88	88	88	57	55	59	57	58	58	59	61	60	60	61	62	62	59
14	83	64	91	63	62	61	66	63	64	65	64	67	66	65	68	65	69
15	88	88	88	47	49	54	55	49	55	58	56	57	57	55	59	57	58
16	91	91	78	67	67	64	64	63	66	64	64	63	63	62	61	66	63
17	88	88	86	57	58	59	59	58	58	55	58	58	47	49	54	55	49
18	78	78	88	60	61	62	62	59	59	66	66	65	67	67	64	64	63
19	86	86	83	66	65	68	65	69	65	58	56	56	57	58	59	59	58
20	88	88	88	57	55	59	57	58	58	59	61	60	60	61	62	62	59

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300MIN	360 MIN	420 MIN	480 MIN	540 MIN
21	83	83	91	57	58	59	59	58	58	65	64	67	66	65	68	65	69
22	88	88	88	60	61	62	62	59	59	58	56	57	57	55	59	57	58
23	91	91	78	66	65	68	65	69	65	58	56	56	57	58	59	59	58
24	88	88	86	57	55	59	57	58	58	59	61	60	60	61	62	62	59
25	78	78	88	63	62	61	66	63	64	65	64	67	66	65	68	65	69
26	86	86	56	57	58	59	59	58	58	56	56	57	58	59	59	58	58
27	88	88	60	60	61	62	62	59	59	61	60	60	61	62	62	59	59
28	83	64	67	66	65	68	65	69	65	64	67	66	65	68	65	69	65
29	88	88	57	57	55	59	57	58	58	56	57	57	55	59	57	58	58
30	91	91	63	63	62	61	66	63	64	64	63	63	62	61	66	63	64
31	78	88	88	60	61	62	62	59	59	58	56	57	57	55	59	57	64
32	86	78	91	66	65	68	65	69	65	58	56	56	57	58	59	59	58
33	88	86	88	57	55	59	57	58	58	59	61	60	60	61	62	62	59
34	83	88	78	63	62	61	66	63	64	65	64	67	66	65	68	65	65
35	88	83	86	47	49	54	55	49	55	58	56	57	57	55	59	57	64
36	91	88	88	67	67	64	64	63	66	64	64	63	63	62	61	66	58
37	88	91	83	57	58	59	59	58	58	55	58	58	47	49	54	55	59
38	78	88	88	60	61	62	62	59	59	66	66	65	67	67	64	64	65
39	86	78	91	66	65	68	65	69	65	58	56	56	57	58	59	59	64
40	88	86	88	57	55	59	57	58	58	59	61	60	60	61	62	62	58
41	83	88	78	57	58	59	59	58	58	65	64	67	66	65	68	65	59
42	88	61	86	60	61	62	62	59	59	58	56	57	57	55	59	57	65

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300MIN	360 MIN	420 MIN	480 MIN	540 MIN
43	91	64	88	66	65	68	65	69	65	58	56	56	57	58	59	59	64
44	88	56	57	57	55	59	57	58	58	59	61	60	60	61	62	62	58
45	78	88	88	63	62	61	66	63	64	65	64	67	66	65	68	65	64
46	86	91	91	57	58	59	59	58	58	56	56	57	58	59	59	58	58
47	88	88	88	60	61	62	62	59	59	61	60	60	61	62	62	59	59
48	83	78	78	66	65	68	65	69	65	64	67	66	65	68	65	69	65
49	88	86	86	63	62	61	66	63	64	64	63	63	62	61	66	63	64
50	91	88	88	57	58	59	59	58	58	56	56	57	58	59	59	58	58

VISUAL ANALOGUE SCORE —INTRATHECAL ISOBARIC 0.75%ROPIVACAINE

S. No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
1	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
2	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
3	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
4	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
5	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
6	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
7	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
8	0	0	0	3	3	3	4	4	4	4	4	4	4	4	4	4	4
9	0	0	0	2	2	3	3	3	3	3	3	3	3	3	4	4	4
10	0	0	0	2	2	3	3	3	3	3	3	3	3	3	4	4	4
11	0	0	0	2	2	2	3	3	3	3	3	3	3	3	4	4	4
12	0	0	0	4	3	4	4	4	4	4	4	4	4	4	4	4	4
13	0	0	0	4	3	4	4	4	4	4	4	4	4	4	4	4	4
14	0	0	0	4	3	4	4	4	4	4	4	4	4	4	4	4	4
15	0	0	0	2	2	3	3	3	3	3	3	3	3	3	4	4	4
16	0	0	0	1	2	3	2	2	2	2	2	2	2	2	4	4	4
17	0	0	0	1	2	3	2	2	2	2	2	2	2	2	4	4	4
18	0	0	0	1	2	2	2	2	2	2	2	2	2	2	4	4	4
19	0	0	0	1	2	2	2	2	2	2	2	2	2	2	4	4	4
20	0	0	0	1	2	3	2	2	2	2	2	2	2	2	4	4	4
21	0	0	0	1	2	3	2	2	2	3	3	3	3	3	4	4	4
22	0	0	0	3	3	3	4	4	4	4	4	4	4	4	4	4	4
23	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
24	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
25	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
26	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
27	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4

28	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
29	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
30	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
31	0	0	0	2	2	2	3	3	3	3	3	3	3	3	4	4	4
32	0	0	0	4	3	4	4	4	4	4	4	4	4	4	4	4	4
33	0	0	0	4	3	4	4	4	4	4	4	4	4	4	4	4	4
34	0	0	0	4	3	4	4	4	4	4	4	4	4	4	4	4	4
35	0	0	0	2	2	3	3	3	3	3	3	3	3	3	4	4	4
36	0	0	0	1	2	3	2	2	2	2	2	2	2	2	4	4	4
37	0	0	0	1	2	3	2	2	2	2	2	2	2	2	4	4	4
38	0	0	0	1	2	2	2	2	2	2	2	2	2	2	4	4	4
39	0	0	0	1	2	2	2	2	2	2	2	2	2	2	4	4	4
40	0	0	0	1	2	3	2	2	2	2	2	2	2	2	4	4	4
41	0	0	0	1	2	3	2	2	2	3	3	3	3	3	4	4	4
42	0	0	0	3	3	3	4	4	4	4	4	4	4	4	4	4	4
43	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
44	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
45	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
46	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
47	0	0	0	2	3	3	3	3	3	3	3	3	3	3	4	4	4
48	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
49	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4
50	0	0	0	4	3	3	4	4	4	4	4	4	4	4	4	4	4

VISUAL ANALOGUE SCORE–GROUP D

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	36O MIN	420 MIN	480 MIN	540 MIN
1	0	0	0	0	0	0	0	1	2	3	3	3	3	3	3	4	4
2	0	0	0	0	0	0	0	1	1	3	2	3	3	3	4	4	4
3	0	0	0	0	0	0	0	1	1	3	3	3	3	3	2	4	4
4	0	0	0	0	0	0	0	1	1	3	3	3	3	3	3	4	4
5	0	0	0	0	0	0	0	1	1	3	3	3	3	3	3	4	4
6	0	0	0	0	0	0	0	1	1	2	3	3	3	3	4	4	4
7	0	0	0	0	0	0	0	1	1	2	2	2	3	3	3	3	4
8	0	0	0	0	0	0	0	1	1	3	3	3	3	3	2	3	2
9	0	0	0	0	0	0	0	1	3	3	3	3	3	2	3	2	4
10	0	0	0	0	0	0	0	1	1	2	2	2	3	2	2	2	4
11	0	0	0	0	0	0	0	1	1	2	2	2	3	3	3	4	4
12	0	0	0	0	0	0	0	1	1	2	2	2	3	3	2	3	4
13	0	0	0	0	0	0	0	1	1	3	3	3	2	3	2	2	4
14	0	0	0	0	0	0	0	1	1	3	3	3	2	2	3	3	4
15	0	0	0	0	0	0	0	1	1	2	3	3	3	3	2	3	4
16	0	0	0	0	0	0	0	1	1	2	3	3	2	3	2	3	2
17	0	0	0	0	0	0	0	1	2	3	3	3	2	2	2	2	2
18	0	0	0	0	0	0	0	1	2	3	3	3	3	3	3	3	3
19	0	0	0	0	0	0	0	1	3	3	3	3	2	3	2	3	2
20	0	0	0	0	0	0	0	1	3	3	3	3	2	2	2	2	2
21	0	0	0	0	0	0	0	1	2	3	3	3	3	3	3	3	3
22	0	0	0	0	0	0	0	1	2	3	2	2	2	3	2	3	2
23	0	0	0	0	0	0	0	1	2	3	2	2	2	2	2	2	2
24	0	0	0	0	0	0	0	1	3	3	3	2	3	3	3	3	3
25	0	0	0	0	0	0	0	1	2	3	2	2	3	3	2	3	2
26	0	0	0	0	0	0	0	1	1	2	3	3	2	3	2	3	2

27	0	0	0	0	0	0	0	1	2	3	3	3	2	2	2	2	2
28	0	0	0	0	0	0	0	1	2	3	3	3	3	3	3	3	3
29	0	0	0	0	0	0	0	1	3	3	3	3	2	3	2	3	2
30	0	0	0	0	0	0	0	1	3	3	3	3	2	2	2	2	2
31	0	0	0	0	0	0	0	1	1	2	2	2	3	3	3	4	4
32	0	0	0	0	0	0	0	1	1	2	2	2	3	3	2	3	4
33	0	0	0	0	0	0	0	1	1	3	3	3	2	3	2	2	4
34	0	0	0	0	0	0	0	1	1	3	3	3	2	2	3	3	4
35	0	0	0	0	0	0	0	1	1	2	3	3	3	3	2	3	4
36	0	0	0	0	0	0	0	1	1	2	3	3	2	3	2	3	2
37	0	0	0	0	0	0	0	1	2	3	3	3	2	2	2	2	2
38	0	0	0	0	0	0	0	1	2	3	3	3	3	3	3	3	3
39	0	0	0	0	0	0	0	1	3	3	3	3	2	3	2	3	2
40	0	0	0	0	0	0	0	1	3	3	3	3	2	2	2	2	2
41	0	0	0	0	0	0	0	1	2	3	3	3	3	3	3	3	3
42	0	0	0	0	0	0	0	1	2	3	2	2	2	3	2	3	2
43	0	0	0	0	0	0	0	1	2	3	2	2	2	2	2	2	2
44	0	0	0	0	0	0	0	1	3	3	3	2	3	3	3	3	3
45	0	0	0	0	0	0	0	1	2	3	2	2	3	3	2	3	2
46	0	0	0	0	0	0	0	1	1	2	3	3	2	3	2	3	2
47	0	0	0	0	0	0	0	1	2	3	3	3	2	2	2	2	2
48	0	0	0	0	0	0	0	1	2	3	3	3	3	3	3	3	3
49	0	0	0	0	0	0	0	1	3	3	3	3	2	3	2	3	2
50	0	0	0	0	0	0	0	1	3	3	3	3	2	2	2	2	2

SATURATION –GROUP R

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	36O MIN	420 MIN	480 MIN	540 MIN
1	98%	99%	99%	98%	99%	99%	98%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
2	98%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
3	99%	99%	98%	98%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
4	98%	98%	97%	98%	98%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
5	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
6	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
7	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
8	100%	100%	100%	100%	100%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
9	100%	100%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
10	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
11	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
12	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
13	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
14	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
15	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
16	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
17	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
18	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
19	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
20	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
21	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
22	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
23	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
24	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
25	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
26	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

27	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
28	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
29	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
30	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
31	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
32	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
33	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
34	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
35	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
36	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
37	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
38	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
39	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
40	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
41	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
42	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
43	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
44	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
45	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
46	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
47	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
48	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
49	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
50	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

SATURATION –GROUP D

S No	420 MIN	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	36O MIN	480 MIN	540 MIN
1	100%	98%	99%	99%	98%	99%	99%	98%	100%	100%	100%	100%	100%	100%	100%	100%	100%
2	100%	98%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
3	100%	99%	99%	98%	98%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
4	100%	98%	98%	97%	98%	98%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
5	100%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
6	98%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	99%	99%	98%
7	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%	99%	99%	99%
8	99%	100%	100%	100%	100%	100%	99%	99%	100%	100%	100%	100%	100%	100%	99%	99%	99%
9	99%	100%	100%	99%	99%	99%	99%	99%	100%	99%	98%	99%	98%	99%	99%	99%	99%
10	98%	99%	98%	99%	98%	99%	99%	99%	100%	99%	99%	99%	99%	99%	99%	99%	98%
11	99%	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	99%	99%	99%	99%	99%	99%
12	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%
13	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	98%	99%	98%	99%	99%	99%	99%
14	98%	99%	98%	99%	98%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	98%
15	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%
16	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%
17	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	98%	99%	98%	99%	99%	99%	99%
18	98%	99%	98%	99%	98%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	98%
19	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%
20	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%
21	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	98%	99%	98%	99%	99%	99%	99%
22	98%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	98%
23	99%	99%	99%	99%	99%	99%	100%	99%	100%	99%	99%	99%	99%	99%	99%	99%	99%
24	99%	99%	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	99%	99%	99%	99%	99%
25	99%	99%	99%	99%	99%	99%	100%	99%	100%	99%	98%	99%	98%	99%	99%	99%	99%
26	98%	99%	99%	99%	99%	99%	99%	99%	99%	98%	99%	98%	99%	98%	99%	99%	98%
27	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%

28	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%
29	99%	99%	99%	99%	99%	99%	100%	99%	99%	99%	99%	99%	99%	99%	99%	99%	99%
30	100%	99%	99%	99%	99%	99%	99%	99%	99%	98%	99%	98%	99%	98%	99%	100%	100%
31	99%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
32	99%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
33	99%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
34	99%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
35	99%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
36	99%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
37	99%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
38	99%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
39	99%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	99%	99%
40	100%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
41	100%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
42	100%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
43	100%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
44	100%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
45	100%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
46	100%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
47	100%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
48	100%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
49	100%	99%	99%	99%	99%	99%	100%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%
50	100%	99%	99%	99%	99%	99%	99%	99%	100%	100%	100%	100%	100%	100%	100%	100%	100%

FOUR POINT VERBAL RATING SCALE –GROUP R

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	36O MIN	420 MIN	480 MIN	540 MIN
1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
17	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
18	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
19	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
20	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
21	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
22	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
23	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
24	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
25	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
26	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

27	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
28	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
29	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
30	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
31	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
32	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
33	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
34	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
35	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
36	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
37	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
38	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
39	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
40	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
41	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
42	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
43	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
44	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
45	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
46	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
47	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
48	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
49	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
50	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

FOUR POINT VERBAL RATING SCALE – GROUP D

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	36O MIN	420 MIN	480 MIN	540 MIN
1	1	1	1	2	2	2	3	3	3	2	2	2	1	1	1	1	1
2	1	1	1	2	2	2	3	3	3	2	2	2	1	1	1	1	1
3	1	1	1	2	2	2	3	3	3	3	3	3	1	1	1	1	1
4	1	1	1	2	2	3	2	2	3	3	2	2	1	1	1	1	1
5	1	1	1	3	3	3	3	3	3	3	2	2	1	1	1	1	1
6	1	1	1	3	3	3	3	3	3	2	2	2	1	1	1	1	1
7	1	1	1	3	3	2	3	2	2	2	3	1	1	1	1	1	1
8	1	1	1	2	2	2	3	3	3	3	3	1	1	1	1	1	1
9	1	1	1	2	2	2	3	3	3	3	3	2	2	2	1	1	1
10	1	1	1	2	2	3	3	3	3	3	3	2	2	2	1	1	1
11	1	1	1	2	2	3	3	3	3	3	3	2	2	2	1	1	1
12	1	1	1	2	2	3	3	3	3	3	3	2	2	2	1	1	1
13	1	1	1	2	2	2	3	3	3	3	3	2	2	2	1	1	1
14	1	1	1	2	2	2	3	3	3	2	2	2	2	2	1	1	1
15	1	1	1	3	3	2	3	2	2	2	2	1	1	1	1	1	1
16	1	1	1	2	3	3	3	3	2	2	2	1	1	1	1	1	1
17	1	1	1	2	3	3	3	3	2	2	2	1	1	1	1	1	1
18	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
19	1	1	1	2	3	2	3	3	3	3	3	2	2	2	1	1	1
20	1	1	1	2	3	2	3	3	3	3	3	2	2	2	1	1	1
21	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
22	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
23	1	1	1	2	3	3	3	3	3	2	2	1	1	1	1	1	1
24	1	1	1	2	3	3	3	3	3	2	2	2	2	2	1	1	1
25	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
26	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1

27	1	1	1	3	3	3	2	2	2	2	2	1	1	1	1	1	1
28	1	1	1	3	3	3	3	3	3	3	3	2	2	2	1	1	1
29	1	1	1	3	3	3	3	3	3	3	3	2	2	2	1	1	1
30	1	1	1	2	2	3	3	3	3	3	3	2	2	2	1	1	1
31	1	1	1	2	2	3	3	3	3	3	3	2	2	2	1	1	1
32	1	1	1	2	2	3	2	2	2	2	2	2	2	2	1	1	1
33	1	1	1	2	3	3	2	2	2	2	2	2	2	2	1	1	1
34	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
35	1	1	1	2	3	3	2	2	2	2	2	1	1	1	1	1	1
36	1	1	1	2	3	3	2	2	2	2	2	1	1	1	1	1	1
37	1	1	1	3	3	3	2	2	2	2	2	1	1	1	1	1	1
38	1	1	1	3	2	3	3	3	2	2	2	2	2	2	1	1	1
39	1	1	1	3	2	3	3	3	2	2	2	2	2	2	1	1	1
40	1	1	1	3	3	3	3	3	2	2	2	2	2	2	1	1	1
41	1	1	1	3	3	3	3	3	2	2	2	2	2	2	1	1	1
42	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
43	1	1	1	2	3	3	3	3	3	2	2	1	1	1	1	1	1
44	1	1	1	2	3	3	3	3	3	2	2	2	2	2	1	1	1
45	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
46	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
47	1	1	1	2	3	3	2	2	2	2	2	1	1	1	1	1	1
48	1	1	1	2	3	3	3	3	3	3	3	2	2	2	1	1	1
49	1	1	1	2	2	3	3	3	3	3	3	2	2	2	1	1	1
50	1	1	1	2	2	3	3	3	3	2	2	2	2	2	1	1	1

MEAN ARTERIAL PRESURE-GROUP R

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
1	110	96	96	87	88	99	99	96	96	87	96	96	101	102	112	121	111
2	119	90	90	80	91	102	102	90	90	80	90	90	108	109	119	126	128
3	111	96	89	99	88	99	99	96	89	99	96	89	111	102	112	121	111
4	117	90	99	99	78	99	96	90	99	99	90	99	105	109	119	126	128
5	116	96	99	99	86	99	98	96	99	99	96	99	106	102	112	121	111
6	100	90	89	99	88	99	94	90	89	99	90	89	107	102	112	121	111
7	109	86	99	99	83	99	92	86	99	99	86	99	108	119	119	126	128
8	108	96	96	87	88	99	99	96	96	87	96	96	101	102	112	121	111
9	109	90	90	80	91	102	102	90	90	80	90	90	108	109	119	126	128
10	120	96	89	99	88	99	99	96	89	99	96	89	105	122	112	121	111
11	108	90	99	99	78	99	96	90	99	99	90	99	111	122	112	121	111
12	126	96	99	99	86	99	98	96	99	99	96	99	128	129	119	126	128
13	121	90	89	99	88	99	94	90	89	99	90	89	111	122	112	121	111
14	126	86	99	99	83	99	92	86	99	99	86	99	128	129	119	126	128
15	111	96	96	87	88	99	99	96	96	87	88	99	111	122	112	121	111
16	126	90	90	80	91	102	102	90	90	80	91	102	101	122	112	121	111
17	121	96	89	99	88	99	99	96	89	99	88	99	108	129	119	126	128
18	107	90	99	99	78	99	96	90	99	99	88	99	111	122	112	121	111
19	105	96	99	99	86	99	98	96	99	99	86	99	108	129	119	126	128
20	106	90	89	99	88	99	94	90	89	99	88	99	106	122	112	121	111

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
21	111	86	99	99	83	99	92	86	99	99	83	99	106	122	112	121	111
22	106	96	96	87	88	99	99	96	96	87	88	99	101	102	101	102	128
23	121	90	90	80	91	102	102	90	90	80	91	102	108	109	108	109	111
24	106	96	89	99	88	99	99	96	89	99	88	99	111	102	111	102	128
25	121	90	99	99	78	99	96	90	99	99	78	99	105	109	105	109	111
26	106	96	99	99	86	99	98	96	99	99	86	99	111	122	112	121	111
27	101	90	89	99	88	99	94	90	89	99	88	99	128	129	119	126	128
28	116	86	99	99	83	99	92	86	99	99	83	99	111	122	112	121	111
29	111	96	96	87	88	99	99	96	96	87	88	99	108	129	119	126	128
30	106	90	90	80	91	102	102	90	90	80	91	102	101	122	112	121	111
31	108	90	99	99	78	99	96	90	99	99	90	99	111	122	112	121	102
32	126	96	99	99	86	99	98	96	99	99	96	99	128	129	119	126	109
33	121	90	89	99	88	99	94	90	89	99	90	89	111	122	112	121	102
34	126	86	99	99	83	99	92	86	99	99	86	99	128	129	119	126	109
35	111	96	96	87	88	99	99	96	96	87	88	99	111	122	112	121	121
36	126	90	90	80	91	102	102	90	90	80	91	102	101	122	112	121	126
37	121	96	89	99	88	99	99	96	89	99	88	99	108	129	119	126	102
38	122	90	99	99	78	99	96	90	99	99	88	99	111	122	112	121	109
39	129	96	99	99	86	99	98	96	99	99	86	99	108	129	119	126	102
40	122	90	89	99	88	99	94	90	89	99	88	99	106	122	112	121	109
41	122	86	99	99	83	99	92	86	99	99	83	99	106	122	112	121	121
42	102	96	96	87	88	99	99	96	96	87	88	99	101	102	101	102	126

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
43	109	90	90	80	91	102	102	90	90	80	91	102	108	109	108	109	102
44	122	96	83	99	92	86	99	99	83	99	88	99	111	102	111	102	109
45	129	90	88	99	99	96	96	87	88	99	78	99	105	109	105	109	102
46	122	96	91	102	102	90	90	80	91	102	86	99	111	122	112	121	109
47	122	90	83	99	92	86	99	99	83	99	88	99	128	129	119	126	121
48	102	86	88	99	99	96	96	87	88	99	83	99	111	122	112	121	126
49	109	96	96	87	88	99	99	96	96	87	88	99	108	129	119	126	102
50	122	90	90	80	91	102	102	90	90	80	91	102	101	122	112	121	109

MEAN ARTERIAL PRESURE-GROUP D

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
1	110	96	96	87	88	89	89	88	90	100	104	98	97	88	89	89	88
2	119	90	90	80	91	75	72	79	80	89	81	90	90	91	92	92	89
3	111	96	89	99	88	60	65	69	88	90	100	104	88	90	68	65	69
4	117	90	99	99	78	61	57	58	79	80	89	81	79	80	59	57	58
5	116	96	99	99	86	67	88	90	100	90	100	104	88	90	61	66	63
6	100	90	89	99	88	60	79	80	89	80	89	81	79	80	54	55	49
7	109	86	99	99	83	68	88	90	100	88	90	100	104	88	90	100	104
8	108	96	96	87	88	67	79	80	89	79	80	89	81	79	80	89	81
9	109	90	90	80	91	60	88	90	100	88	90	100	104	88	90	100	104
10	120	96	89	99	88	59	79	80	89	79	80	89	81	79	80	89	81
11	108	90	99	99	78	62	88	90	100	88	90	100	104	88	90	100	104
12	126	96	99	99	86	68	65	69	79	79	80	89	81	79	80	89	81
13	121	90	89	99	88	59	67	75	78	88	90	100	104	88	90	100	104
14	126	86	99	99	83	61	66	63	64	65	64	67	86	95	98	95	109
15	111	96	96	87	88	68	68	65	69	79	79	80	68	88	95	97	101
16	126	90	90	80	91	67	59	67	75	78	88	90	67	96	98	95	102
17	121	96	89	99	88	68	68	65	69	79	79	80	68	95	98	95	99
18	107	90	99	99	78	67	59	67	75	78	88	90	86	95	98	95	109
19	105	96	99	99	86	68	68	65	69	79	79	80	68	88	95	97	101
20	106	90	89	99	88	67	59	67	75	78	88	90	67	96	98	95	102
21	111	86	99	99	83	61	59	58	58	65	64	67	68	95	98	95	49
22	106	96	96	87	88	65	62	59	59	58	56	57	86	95	98	95	109
23	121	90	90	80	91	60	65	69	65	58	56	56	68	88	95	97	101
24	106	96	89	99	88	61	57	58	58	59	61	60	67	96	98	95	102
25	121	90	99	99	78	65	66	63	64	65	64	67	76	85	78	85	89
26	106	96	99	99	86	60	59	58	58	86	95	98	95	109	86	95	98

S No	0 MIN	3 MIN	5 MIN	10 MIN	15 MIN	20 MIN	25 MIN	30 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN	360 MIN	420 MIN	480 MIN	540 MIN
27	101	90	89	99	88	61	62	59	59	68	88	95	97	101	78	88	95
28	116	86	99	99	83	65	65	69	65	67	96	98	95	102	87	96	98
29	111	96	96	87	88	60	57	58	58	68	95	98	95	49	68	95	98
30	106	90	90	80	91	61	66	63	64	86	95	98	95	109	86	95	98
31	108	90	99	99	78	62	88	90	100	88	90	100	104	88	90	100	104
32	126	96	99	99	86	68	65	69	79	79	80	89	81	79	80	89	81
33	121	90	89	99	88	59	67	75	78	88	90	100	104	88	90	100	104
34	126	86	99	99	83	61	66	63	64	65	64	67	86	95	98	95	109
35	111	96	96	87	88	68	68	65	69	79	79	80	68	88	95	97	101
36	126	90	90	80	91	67	59	67	75	78	88	90	67	96	98	95	102
37	121	96	89	99	88	68	68	65	69	79	79	80	68	95	98	95	99
38	122	90	99	99	78	67	59	67	75	78	88	90	86	95	98	95	109
39	129	96	99	99	86	68	68	65	69	79	79	80	68	88	95	97	101
40	122	90	89	99	88	67	59	67	75	78	88	90	67	96	98	95	102
41	122	86	99	99	83	61	59	58	58	65	64	67	68	95	98	95	49
42	102	96	96	87	88	65	62	59	59	58	56	57	86	95	98	95	109
43	109	90	90	80	91	60	65	69	65	58	56	56	68	88	95	97	101
44	122	96	83	99	92	61	57	58	58	59	61	60	67	96	98	95	102
45	129	90	88	99	99	65	66	63	64	65	64	67	76	85	78	85	89
46	122	96	91	102	102	60	59	58	58	86	95	98	95	109	86	95	98
47	122	90	83	99	92	61	62	59	59	68	88	95	97	101	78	88	95
48	102	86	88	99	99	65	65	69	65	67	96	98	95	102	87	96	98
49	109	96	96	87	88	60	57	58	58	68	95	98	95	49	68	95	98
50	122	90	90	80	91	61	66	63	64	86	95	98	95	109	86	95	98

SIDE EFFECTS – GROUP R

S.No	Hypotension	Bradycardia	Nausea	Voiting	Shivering	Dry mouth
1	NO	YES	NO	NO	NO	NO
2	NO	NO	NO	NO	NO	NO
3	NO	NO	NO	NO	YES	NO
4	NO	NO	NO	YES	YES	NO
5	NO	NO	NO	YES	YES	NO
6	YES	NO	NO	YES	YES	NO
7	NO	NO	NO	YES	YES	NO
8	NO	NO	NO	YES	YES	NO
9	NO	NO	NO	YES	NO	NO
10	YES	NO	NO	YES	YES	NO
11	NO	NO	NO	NO	YES	NO
12	NO	NO	NO	NO	YES	NO
13	NO	NO	NO	NO	YES	NO
14	NO	NO	NO	NO	YES	NO
15	NO	NO	NO	NO	YES	NO
16	NO	NO	NO	NO	YES	NO
17	NO	NO	NO	NO	NO	NO
18	NO	NO	NO	NO	NO	NO
19	NO	NO	NO	NO	NO	NO
20	NO	NO	NO	NO	NO	NO
21	NO	NO	NO	NO	NO	NO
22	NO	NO	NO	NO	NO	NO
23	NO	NO	NO	NO	NO	NO
24	NO	NO	NO	NO	NO	NO
25	NO	NO	NO	NO	NO	NO
26	NO	NO	NO	NO	NO	NO
27	NO	NO	NO	NO	NO	NO
28	NO	NO	YES	NO	NO	NO
29	YES	NO	YES	NO	NO	NO
30	YES	NO	YES	NO	NO	YES
31	NO	NO	NO	NO	YES	NO
32	NO	NO	NO	NO	YES	NO
33	NO	NO	NO	NO	YES	NO
34	NO	NO	NO	NO	YES	NO
35	NO	NO	NO	NO	YES	NO
36	NO	NO	NO	NO	YES	NO
37	NO	NO	NO	NO	NO	NO
38	NO	NO	NO	NO	NO	NO
39	NO	NO	NO	NO	NO	YES
40	NO	NO	NO	NO	NO	NO
41	NO	NO	NO	NO	NO	NO
42	NO	NO	NO	NO	NO	NO
43	NO	NO	NO	NO	NO	NO
44	NO	NO	NO	NO	NO	NO
45	NO	NO	NO	NO	NO	NO
46	NO	NO	NO	NO	NO	NO
47	NO	YES	YES	NO	NO	NO
48	NO	NO	YES	NO	NO	NO
49	YES	NO	YES	NO	NO	NO
50	YES	YES	YES	NO	NO	NO

SIDE EFFECTS – GROUP D

S. No	Hypotension	Bradycardia	Nausea	Vomiting	Shivering	Dry mouth
1	NO	NO	NO	NO	NO	NO
2	NO	YES	NO	NO	NO	NO
3	NO	NO	YES	YES	NO	NO
4	NO	NO	NO	NO	NO	NO
5	NO	NO	NO	NO	NO	NO
6	NO	NO	NO	NO	NO	NO
7	NO	NO	NO	NO	NO	NO
8	NO	NO	NO	NO	NO	NO
9	NO	NO	NO	NO	NO	NO
10	NO	NO	NO	NO	NO	NO
11	NO	NO	NO	NO	NO	NO
12	NO	NO	NO	NO	NO	NO
13	NO	NO	NO	NO	NO	NO
14	NO	NO	NO	NO	NO	NO
15	NO	NO	NO	NO	NO	NO
16	NO	YES	YES	YES	NO	NO
17	NO	NO	NO	NO	NO	NO
18	NO	YES	NO	NO	NO	YES
19	NO	YES	NO	NO	NO	YES
20	YES	NO	NO	NO	NO	YES
21	NO	NO	NO	NO	NO	NO
22	NO	NO	NO	NO	NO	NO
23	YES	NO	NO	NO	NO	NO
24	NO	NO	NO	NO	NO	NO
25	NO	NO	NO	NO	NO	NO
26	YES	NO	NO	NO	NO	NO
27	NO	NO	NO	NO	NO	NO
28	NO	NO	NO	NO	NO	NO
29	YES	NO	NO	NO	NO	NO
30	NO	NO	NO	NO	NO	NO
31	NO	NO	NO	NO	NO	NO
32	NO	NO	NO	NO	NO	NO
33	NO	NO	NO	NO	NO	NO
34	NO	NO	NO	NO	NO	NO
35	NO	NO	NO	NO	NO	NO
36	NO	YES	YES	YES	NO	NO
37	YES	NO	NO	NO	NO	NO
38	NO	YES	NO	NO	NO	NO
39	NO	YES	NO	NO	NO	NO
40	YES	NO	NO	NO	NO	NO
41	NO	NO	NO	NO	NO	NO
42	NO	NO	NO	NO	NO	NO
43	YES	NO	NO	NO	NO	NO
44	NO	NO	NO	NO	NO	NO
45	NO	NO	NO	NO	NO	NO
46	YES	NO	NO	NO	YES	NO
47	NO	NO	NO	NO	NO	NO
48	NO	NO	NO	NO	NO	NO
49	YES	NO	NO	NO	YES	NO
50	NO	NO	NO	NO	NO	NO